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FURTHER EXPERIENCE WITH REGIONAL ENTERITIS

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BOSTON

IN 1935 our experience with 11 cases of regional ileitis was reported by one of us[1] and it was concluded that extirpation of the diseased bowel was the most effective treatment. Recently the soundness of this conclusion has been questioned, because of recurrence following what appeared to be adequate intestinal resection. We have now had an opportunity to study and treat 20 cases of this disease, and feel that conclusions from their careful analysis should prove an aid in standardizing the procedure for early diagnosis and subsequent management.

RACE AND AGE

Although in most reported series the majority of patients are Jews, 3 of ours were not. This is essentially a disease of youth; 11 patients were under twenty-five and 7 were between twenty-five and thirty-five. The youngest was fourteen, the oldest fifty-six.

ETIOLOGY AND LOCATION

Homans and Hass[2] thought that primary infection of the appendix spreading to the ileum might explain the condition, while Felsen and Gorenberg,[3] from their observations of a number of cases which developed after an epidemic of bacillary dysentery, concluded that there was an etiologic relation between these two diseases. Crohn and Rosenak,[4] however, were able to find evidence of bacillary dysentery by agglutination tests in only 1 case. Jackson[9] considers that mesenteric lymphadenitis is related to regional enteritis, "both possibly being due to low-grade infection of the lymphatic system." Reichert and Mathes[5] produced chronic lymphedema of the bowel in dogs by injecting sclerosing material into the mesenteric and subserosal lymphatic vessels. Thickening and edema of the bowel wall similar to that seen in chronic regional enteritis resulted. When bacteria were injected intravenously in conjunction with the lymphatic injection, a greater thickening of the intestinal wall occurred; this was apparently a permanent pathologic alteration. These investigators suggest that there is a close resemblance between the pathologic changes in chronic regional enteritis and those in experimental intestinal lymphedema. They attribute the extensive fibrosis and mucosal ulceration seen in the former condition to the presence of a chronic low-grade bacterial infection. The observations of Homans, Drinker and Field[6] that the streptococcus may produce lymphatic obstruction leading to lymphedema of the lower extremities lend credence to the conclusions of Reichert and Mathes. Probstein and Gruenfeld[7] think that the greater frequency of involvement of the terminal ileum may be due to its rich lymphatic supply, which with stagnation at the ileocecal valve favors bacterial absorption.

Usually the lesions are so advanced when seen at operation that a mixed culture of organisms is obtained. In 1 early case, operation disclosed an excess of straw-colored peritoneal fluid; cultures from this fluid, from the cut surface of the involved mesenteric lymph nodes and from the deep surface of the intestinal ulcerations, all yielded an anaerobic streptococcus in pure culture. Repeated efforts by the appropriate bacteriological methods have not demonstrated the tubercle bacillus in any case. Further clinical and experimental data are necessary to establish the etiology definitely.

The lesion most often involves the terminal ileum, stopping abruptly at the ileocecal valve, where the process shows its greatest activity. Recently a number of cases involving other parts of the small and the large intestine have been reported. In our own group of cases, 3 presented separate involvement of the ileum and colon. In some cases, various parts of the small and large intestine were involved by contiguity with the terminal ileum; so that the term "regional enteritis" or "chronic cicatrizing enteritis" more accurately

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describes the condition than does "regional ileitis," the name by which the disease is commonly known.

CLINICAL FEATURES AND PATHOLOGY

Regional enteritis is a progressive disease extending over months or years, and tending to fall into four different phases corresponding to the degree of involvement. The symptoms and signs depend largely on location, extent, duration and severity of the disease.

The first stage is that of an acute intra-abdominal lesion, with signs and symptoms of peritoneal irritation. Acute pain in the right lower quadrant, vomiting, slight fever, leukocytosis and abdominal tenderness and spasm may be present. This stage resembles acute appendicitis, and half our patients gave a history of appendectomy without relief of symptoms. At operation an excess of free peritoneal fluid is found, and a reddened, thickened terminal ileum is seen. The appendix usually lacks evidence of primary acute inflammation. Enlarged mesenteric lymph nodes are invariably present. In 3 of our cases this condition was found; in each it was felt that the mildness of the disease did not warrant resection, and nothing more than incidental appendectomy was done. The subsequent course in these cases will be further described.

As the disease advances symptoms appear resembling those of mild, idiopathic ulcerative colitis: frequent loose bowel movements, recurring bouts of fever, crampy abdominal pains, progressive weakness and marked loss of weight; but there is no tenesmus. The physical examination discloses lower abdominal tenderness, and a mass may be palpated by abdominal or rectal examination, but proctoscopic examination fails to show the usual lesions of ulcerative colitis in the lower bowel. Anemia and leukocytosis are commonly present. Gross or microscopic blood in the stool is not ordinarily found, but it may occur. It is in this stage that ileocecal tuberculosis, typhoid, paratyphoid, undulant fever and lymphoblastoma may be considered in the differential diagnosis.

At operation the terminal ileum is found thickened and edematous, with corresponding involvement of the mesenteric lymph nodes. When the specimen is cut open, many ulcerations are found in the mucosa of the diseased bowel. About half our cases presented a picture corresponding to this phase.

The third phase is that of chronic partial intestinal obstruction. As a result of extreme thickening of the bowel wall and healing of its mucosal ulcerations, the lumen of the intestine gradually narrows. The constriction is most marked in the region of the ileocecal valve. Severe cramps, nausea, vomiting and constipation are frequent complaints. A mass is nearly always palpable at this stage. Three such cases are included in our series.

The fourth phase of the disease is characterized by the development of multiple sinuses and fistulas. These result from slow perforation of the mucosal ulcers. The diseased bowel and its mesentery are enormously thickened and doughy, presenting what has been described as a soggy, hose-like ileum. Sinuses may be present between the terminal ileum and other coils of bowel or the abdominal wall. Walled-off abscesses may be found between loops of bowel. Numerous hyperplastic mesenteric lymph nodes are often seen. The cut surface of the intestinal wall shows clear definition of layers due to diffuse edema, most marked in the submucosa and serosa. The mucosal surface loses its villous fringes, showing instead a shiny, cobblestone-like surface with numerous superficial ulcers which tend to concentrate along the mesenteric border. External fistulas may be present, especially when appendectomy has been done previously; in such cases a chronic draining sinus or fecal fistula may persist indefinitely, resisting all efforts at closure until resection of the diseased bowel is carried out. In 4 of our cases persistent external fecal fistulas had become established following laparotomy. In 7 cases internal fistulas were present.

Microscopically the process shows a low-grade inflammatory reaction characterized by widespread edema and a mild cellular reaction with lymphocytes, plasma cells, monocytes and a few eosinophils. There is a little or no fibrin or polymorphonuclear reaction except in the region of the ulcers or sinuses. Minute, scattered areas of necrosis which have become transformed into epithelioid tubercles may be seen, but they differ from the picture of tuberculosis in the absence of the monocytic reaction around the multinuclear giant cells.

The duration of the symptoms varied from two weeks in 1 early case to four years in 3 cases. The average duration before the diagnosis was made and surgical therapy instituted was sixteen months. The triad of colicky abdominal pain, diarrhea and weight loss occurred in the largest number of cases.

COMPLICATIONS

Conceivably some early cases of regional enteritis heal with spontaneous recovery. Untreated cases commonly develop the complications already noted, such as sinuses and internal or external fistulas. Although chronic partial intestinal obstruction is frequently present, acute obstruction seems to be a rare complication. Perforation of an ulcer into

the free peritoneal cavity with fatal generalized peritonitis has been reported.

Single and multiple, intraperitoneal and extraperitoneal abscesses have been observed. In 1 of our cases, the patient developed portal pylephlebitis with multiple liver abscesses, as well as a subphrenic abscess, and only the postmortem examination disclosed the origin of the suppurative phlebitis to be a regional enteritis. In another patient a fistula between bowel and bladder gave rise to severe urinary sepsis. Marked anemia, peripheral neuritis and nutritional edema are among the other late complications.

DIAGNOSIS

The diagnosis of regional enteritis should be considered whenever a young adult complains of symptoms suggestive of partial intestinal obstruction, particularly if there is evidence of an associated low-grade inflammatory process. A history of colicky abdominal pain and irregular bowel habits, together with loss of weight, slight fever, leukocytosis and anemia, is highly suggestive. The finding of a palpable mass by abdominal or rectal examination is important additional evidence.

Valuable confirmatory evidence is furnished by the x-ray examination. In the early stages the roentgenogram may reveal no typical abnormality, but as the obstructive form develops definite changes may be noted in the small intestine. A filling defect appears in the terminal ileum with stasis and distention proximal to it. In cases in which the stenosis is even more marked the lumen shows merely as a fine line of barium, which Kantor[8] described as the "string sign." Gastrointestinal films taken at hourly intervals are usually necessary to reveal these changes. The barium enema sometimes discloses pressure defects caused by a mass of adherent small bowel or the presence of interintestinal fistulas.

TREATMENT

As Jackson[9] points out, proper surgical treatment is still unsettled, and cannot be determined until the late results of operated cases have been further studied. At present the stage of the disease and the condition of the patient should govern the treatment (Table 1). Cases of acute regional enteritis with spontaneous cure probably do occur. In 3 of our patients the disease was considered to be sufficiently mild so that extensive surgical treatment was inadvisable. In most of the cases encountered, however, the lesions were advanced and progressive. In these, surgical extirpation of the lesion seemed definitely indicated.

There are certain hazards attendant upon radical surgical procedures. Operative manipulation may activate latent infection and cause fatal peritonitis or septicemia. The operation may be rendered extremely difficult by hemorrhage from a thick, friable, edematous mesentery. The presence of complicating fistulas further adds to the risk.

Meyer[10] believes that if the inflammation is limited to the terminal ileum and if the mesentery is not involved to any degree, resection may not be necessary, and Jackson[9] questions the advisability of subjecting poor surgical risks to the hazards of resecting considerable portions of the small or large intestine. He believes it would be well to allow sufficient time to elapse to observe what course the disease is following.

Table 1. *Classification of Cases According to the Stage of the Disease and to Treatment.*

NO. OF CASES	STAGE OF DISEASE	TREATMENT
3	Early	Exploratory laparotomy, appendectomy
1	Moderately advanced	Appendectomy (refused resection)
8	Advanced	One-stage ileocecal resection
7	Advanced	Multiple-stage procedures
1	Advanced: suppurative pylephlebitis and liver abscess	Intestinal lesion not treated surgically

In view of the complications which have been reported and those which we have encountered, resection of the involved intestine in one or more stages seems at present to be the best form of treatment. However, as many of the patients present themselves with definite obstructive symptoms or with fistulas or abscesses, graded procedures, such as drainage of the abscess followed by ileocolostomy and subsequent resection, are sometimes advisable.

When multiple areas of small or large intestine are involved, it may be necessary to carry out more than one sidetracking operation. Our best results have been obtained in the cases in which a one-stage ileocecal resection could be performed and the abdomen closed without drainage. Obviously this type of operation is more readily applicable to the stages of the diseases in which complications are minimal. Conservative operations in early cases do not seem advisable, and we have observed no case in which cure was accomplished without resection of the diseased bowel.

An important step in the prevention of recurrence, we believe, is wide excision of the involved mesentery and its lymph nodes. If the disease originates in the mesenteric lymphatics, as has been suggested, — clinically and experimentally, — it is altogether possible that failure to carry out excision may bear a relation to the recurrences observed by some surgeons.

X-ray therapy has been suggested as an alternate

form of treatment. We have had no experience with this type of treatment. It appears to us not to have a logical basis.

MORTALITY AND FOLLOW-UP

The mortality in the 15 cases subjected to extensive surgical treatment is given in Table 2. The high mortality in the second group is undoubtedly due to the poor condition of the patient and the presence of dangerous complications.

Table 2. *Mortality.*

NO. OF CASES	OPERATION	DEATHS	MORTALITY %
One-stage ileocecal resection...	8	1	13
Multiple-stage procedures.....	7	3	43

The causes of death were peritonitis, septicemia and postoperative pulmonary complications.

A careful inquiry as to the health of the patients who survived resection of the involved bowel has disclosed evidence of recurrence of the disease in only 1 case: a patient whose terminal ileum and sigmoid colon were resected eight months ago now has evidence of disease below the anastomosis. In 2 patients the follow-up period has been five and six years, while in the remainder from six months to four years has elapsed since operation. All these patients are symptom free. They have gained weight, in some cases from 20 to 80 lb. The patient who refused extensive surgical therapy has improved to a moderate degree. This patient is a physician who carries on a fairly active practice, having an occasional exacerbation of abdominal pain and diarrhea. The 3 patients who had early disease and in whom resection was not performed have not been followed for a sufficient time to draw conclusions as to end results.

SUMMARY AND CONCLUSIONS

An analysis of our experience with 20 cases of regional enteritis is presented.

Although the etiology of the disease is not definitely known, evidence favors a low-grade infection of the lymphatic system, possibly related to mesenteric lymphadenitis.

The signs and symptoms depend on the stage, location, extent and severity of the disease. The most important symptoms are colicky abdominal pain, diarrhea, constipation and vomiting, loss of weight and slight fever. In the later stages a mass is palpable. The diagnosis may be confirmed by characteristic x-ray findings.

The disease is usually progressive, with a tendency to develop partial intestinal obstruction, fistulas, abscesses and other dangerous complications.

The most satisfactory treatment at present is surgical, and the preferable operative attack is a one-stage resection of the involved bowel and mesentery, although multiple-stage operations are indicated in complicated cases.

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THE PLACENTAL TRANSFER OF SULFANILAMIDE

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SULFANILAMIDE has gained a place of pre-eminent importance in the treatment of many types of bacterial infection, and in general, the contraindications to its use have been conspicuous by their absence. Its administration during pregnancy, however, to be justifiable, must have a negligible effect on the fetus. At the Boston Lying-in Hospital the drug has been used for some time in the treatment of pyelitis and streptococcic infections occurring during pregnancy. There has been some hesitancy, however, in using it in women at full term as nothing was known concerning the placental transfer of the drug, or its effects upon infants in the immediate neonatal period. The cyanosis appearing in a large percentage of patients receiving therapeutic doses of the drug suggested that the fetal oxygen supply might be compromised if the drug were given just before or during labor. Several investigators[1-4] have shown that this cyanosis is due to methemoglobinemia or occasionally to sulfhemoglobinemia. As shown below, a patient may be markedly cyanotic from the drug without showing any decrease in oxygen saturation.

A complete study of the effects of the drug on infants in utero just prior to delivery is needed. As an initial effort in this direction, the placental transfer of the drug was determined in a small number of cases, and the results are herewith reported.

Women entering the hospital in labor and suffering from infectious processes, such as upper respiratory infections or prolonged rupture of the membranes with fever, were given small divided doses of Prontylin by mouth. The interval between dosage and delivery was carefully noted. At delivery, samples of maternal venous blood and of umbilical-vein blood were collected simultaneously and analyzed for free sulfanilamide content, according to the method of Marshall.[5, 6] The results are recorded in Table 1.

It is to be seen from these figures that sulfanilamide given orally to the mother in labor is found in almost equal concentrations in maternal and fetal venous bloods. The placenta is apparently freely permeable to the drug, and fetal complications from excessive maternal dosage are theoretically possible.

No complications occurred in any of the infants of this group. The doses administered, however, were small in comparison with those that would be necessary in the treatment of severe maternal infections. One patient who had received Prontylin therapy without our knowledge before entry into the hospital was given a total of 100 gr. within thirty hours of delivery. She became deeply cyanotic shortly before delivery. Her infant was born normally, breathed and cried at once, and showed no cyanosis or other abnormalities during its hospital stay. The oxygen capacity of the mother's blood was over 14 vol. per cent, a normal figure.

Table 1. *Summary of Data.*

Case No.	Dosage of Prontylin — Hours before delivery					Sulfanilamide Content	
	17-40	9-16	5-8	3-4	0-2	Maternal venous blood	Fetal venous blood
	gr.	gr.	gr.	gr.	gr.	mg. %	mg. %
1					40		2.5
2	20	20			20	1.4	1.4
3					40	2.5	2.8
4		15	15	25		4.3	4.6
5			15			1.3	1.1
6	60					1.6	2.4
7			20		20	1.5	1.3
8					15	1.1	0.9
9		30	15			3.7	3.7
10	60	20			20	8.9	7.0
11			20			1.2	1.1
12			40	20	20	4.1	3.6
13	80					1.5	1.3
14					20	4.8	2.1
15					40	1.3	0.9
16					20	1.5	0.5
17					20	1.1	0.9

CONCLUSIONS

Sulfanilamide given to pregnant women shortly before or during labor is absorbed in the gastrointestinal tract and passes readily through the placenta to appear in almost equal concentrations in maternal and fetal venous bloods.

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PROGRESS IN GASTROENTEROLOGY IN 1936 AND 1937

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IN REVIEWING the literature on gastroenterology for 1936 and 1937, it becomes apparent that no outstanding developments have occurred in this field. A statement of this kind is always somewhat depressing to those whose major interest is in gastroenterology. This becomes particularly marked when the fair-minded gastroenterologist has to admit that progress in the knowledge of other parts of the body, notably the cardiovascular and pulmonary systems, has been more rapid. In spite of this, there is a brighter side to the picture. Investigation shows that the diagnosis and treatment of the recognized organic disorders of the gastrointestinal tract compare well with those of other systems. The solution of the problem depends in reality upon the frequency of the so-called functional disturbances called into being by disorders in almost any other part of the body. It is obvious that much time must pass and painstaking work be done before this very complicated puzzle is solved.

Much of the literature having to do with the gastrointestinal tract can be best considered under general headings, since it relates to the tract as a whole.

DEFICIENCY DISEASES

The deficiency diseases interest the gastroenterologist because of the dual relation which exists between the vitamins and the intestines. The condition of the stomach and intestines may determine how effectively the vitamins can be utilized, whereas an inadequacy of vitamins may effect changes in the tract.

Minot (Am. J. Digest. Dis. & Nutrition *3*: 643-646, 1936), in a synopsis on anemia and the gastrointestinal tract, gives an excellent summary of some of the problems confronting the profession in regard to the interaction between the stomach and food. Klodt (Med. Welt. *10*: 477-478, 1936) believes that an inadequacy of bile may decrease the absorption of cevitamic acid. Bile considerably retards the oxidation of dilute solutions of cevitamic acid and thus facilitates their absorption from the small intestine. It has been generally recognized that infections decrease the utilization of the vitamins, and Heymann (Am. J. Dis. Child. *51*: 273-283, 1936) suggests that the deficiency in absorption of carotene in children under these conditions may be the result of a disturbed intestinal function.

Stepp (München. med. Wchnschr. *83*: 1119-1123, 1936) has summarized our present knowledge on the changes which occur in the intestines from an insufficient intake of vitamins.

It is now generally recognized that chronic alcoholic neuritis results from an insufficiency of the vitamin B complex. Villaret and his co-workers (Bull. et mém. Soc. méd. d. hôp. de Paris *52*: 1155-1159, 1936) believe that the gastritis so commonly seen in chronic alcoholics is also the result of a deficiency. They observed the presence of some gastritis in 50 of the patients with polyneuritis, and were able to demonstrate an abnormality of the gastric secretion in 45 of them. Thirty-three showed an achlorhydria and 12 showed a marked hypochlorhydria. The gastroscope revealed an atrophic gastritis and an inadequacy of peristalsis in the more advanced cases. Joffe and Jolliffe (Am. J. M. Sc. *193*: 501-510, 1937) have found also a high percentage of alcoholics with an inadequate gastric secretion. However, these authors believe that the inadequate secretion is the direct result of the polyneuritis.

Narat and Loef (Arch. Int. Med. *60*: 449-453, 1937) suggest that the apparent influence of vitamin B_1 on tone and peristalsis is the result of impurities rather than of the vitamin itself. They studied the effect of vitamin B_1 on 8 dogs. An intravenous injection of vitamin B_1 concentrate increased the tone markedly in some instances, while the frequency and amplitude of the movements increased in others. Because their observations suggested that the vitamin concentrate contained histamine and choline, they attempted to eliminate the depressor substances. Following this treatment, the concentrate exhibited no stimulating effect on intestinal contractions. They conclude therefore that the stimulation was due to the presence of histamine and possibly choline, and believe that it remains a matter of conjecture whether intestinal atony is a direct result of vitamin B_1 deficiency.

Recent studies on pellagra and sprue give a better understanding of the effect which these deficiency diseases have on the stomach and intestines. According to Miller and Rhoads (Am. J. M. Sc. *191*: 453-456, 1936), sprue produces the following morphologic changes in the small intestine which can be observed by the x-ray:

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Segmental distribution of barium.

A variation in the contour and caliber of the intestine and segmental contents.

A distorted mucosal pattern, especially of the duodenum and jejunum, but often of the ileum as well.

An outline of the terminal ileum, which appears straighter than normal and gives the impression of lack of pliability.

Furthermore, there appears to be a correlation between the severity of the disease and the extent of the intestinal alteration (Miller and Barker, Arch. Int. Med. *60*: 385-414, 1937).

In 50 cases of severe endemic pellagra studied by Spies et al. (J. A. M. A. *108*: 853-857, 1937), glossitis was present in 41, stomatitis in 33, diarrhea in 29, vomiting in 28 and an achylia gastrica in 15 (of 38) patients.

Thaysen has already suggested that sprue, idiopathic steatorrhea and celiac disease are of the same nature, and Hanes and McBryde (Arch. Int. Med. *58*: 1-16, 1936) assent. The latter report 9 cases of celiac disease which had the sprue syndrome. The description of the stools in both children and adults is very similar. The chief difference between the diseases is found in the blood. The typical anemia of celiac disease is hypochromic and only rarely becomes hyperchromic and macrocytic, whereas the anemia of sprue is at first hypochromic and later becomes hyperchromic and macrocytic. However, the adult sufferer from sprue exhibits the counterpart of the disease seen in children with celiac disease.

PHARMACOLOGY

The recognition of the chemical transmission of impulses from the nerve ends has stimulated clinicians to investigate further the effect of the autonomic nerves on the gastrointestinal tract. Some striking and rather unexpected findings have been reported. For example, Necheles and his coworkers (Am. J. Physiol. *114*: 695-699, 1935-36; Arch. Surg. *33*: 187-196, 1936) found that perfusing the gastric vessels of the rat with a 1: 2,000,000 solution of acetylcholine caused constriction and decreased the rate of perfusion by 10 per cent, in contradistinction to the production of a vasodilatation when the leg vessels were perfused. Acetylcholine also caused constriction of the gastric vessels of the dog. It seemed to enhance the action on the intestines of physostigmine. In doses of 0.025 mg. it had no effect, but combined with 1 mg. of physostigmine produced peristalsis in the stomach, small intestine and colon in almost all animals.

Myerson et al. (New Eng. J. Med. *215*: 1005-1013, 1936) have studied the effect of numerous drugs, such as, Mecholyl, Benzedrine Sulfate, atropine sulfate, physostigmine and Prostigmin, on the gastric secretion. They found that an injection of 25 mg. of Mecholyl caused a marked increase in volume and a great increase in mucin, and within two to eight minutes there developed an alkaline reaction with the production of a marked "acid deficit." However, Benzedrine Sulfate in 40-mg. doses increased free hydrochloric acid, the total acids and pepsinogen, whereas pepsinogen disappeared after Mecholyl. There was no production of mucin. The quantity of juice was not altered. The effect of Benzedrine Sulfate on the gall bladder has been studied in 8 cases (New Eng. J. Med. *216*: 694-697, 1937). There was no evidence that the drug caused any contraction of the gall bladder, and if it was given before a fatty meal it delayed contraction.

In contrast to Myerson's findings that Mecholyl produced an achlorhydria in human beings, Schnedorf and Ivy (Am. J. Digest. Dis. & Nutrition *4*: 429-432, 1937) reported that it caused a stimulation of hydrochloric acid. In several monkeys an unexplained gastric anacidity after histamine lasted from two to five months. This anacidity disappeared suddenly after the administration of Mecholyl, and they believed that the abruptness of this appearance of free acid might be the result of the powerful parasympathetic stimulant's awakening a latent or dormant acid-secreting mechanism. More recently Gray and Ivy (Am. J. Physiol. *120*: 705-711, 1937) have shown that the effect of the drug varied with the dose used. A smaller dose causes a secretion of acid, whereas large doses cause a secretion of alkaline juices.

Pharmacological experiments require special attention to the variations in effects produced by large and small doses. It is a well-known pharmacological phenomenon that the effect of large doses of certain drugs is frequently the direct opposite from results produced by small doses. However, the above reports suggest that the parasympathetic and sympathetic nerves may have mixed effects, and that one cannot be sure of a single reaction from stimulation of any single group of nerves.

This is further brought out in Brown's (Physiol. Rev. *17*: 485-513, 1937) summary of what is now known about the transmission of nerve endings by acetylcholine. It appears necessary to classify the autonomic nervous system on the basis of its chemical action in addition to a parasympathetic and sympathetic division. Thus the effect of choline esters, among which acetylcholine has been particularly studied, can be divided into two groups: a muscarine-like action and a nicotine-like action. As a result of the study of chemical transmission of nerve endings, it becomes obvious that the parasympathetic and sympathetic systems

overlap each other in their effects; thus, some cholenergic fibers probably run in the sympathetic supply to the stomach.

The close relation which exists between the gastrointestinal tract and the blood has been emphasized by the splendid work done by hematologists during the last few years. This work is so important that gastroenterologists and general practitioners alike should be familiar with it. Dameshek (New Eng. J. Med. *218*: 15-38, 1938) has given an adequate review of most of this work, and the reader is referred to his article. It is essential that the physician do complete blood studies on every patient with gastrointestinal symptoms, not only because the existence of an anemia should be recognized and treated, but also because of the aid which the type of anemia may give to the diagnosis.

Studies have been continued on the relation between the gastrointestinal tract and pernicious anemia (see Dameshek). There has been an increasing interest in the anemias associated with diseases of the liver. Clinical studies show that macrocytic anemia is a fairly common finding. Rosenberg (Am. J. Digest. Dis. & Nutrition *3*: 639-643, 1936) studied the blood of 66 selected patients in whom the diagnosis of liver disease seemed beyond question. Forty-two had hypertrophic portal cirrhosis, 4 atrophic portal cirrhosis, 3 hypertrophic biliary cirrhosis, 1 acute yellow atrophy, 10 toxic hepatitis, 3 carcinoma of the head of the pancreas and 3 diffuse metastatic carcinoma of the liver. The authors found a macrocytic anemia in 58 cases (88 per cent). Of the remaining 8, a normocytic, normochromic anemia was present in 2 patients with hypertrophic and in 1 with atrophic cirrhosis. Hemoglobin studies were made only with the Sahli hemoglobinometer; they were difficult to read owing to the presence of bile. Wintrobe (Arch. Int. Med. 57: 289-306, 1936) states that either a normocytic or macrocytic anemia may be present and that the macrocytic type is morphologically similar to, if not identical with, pernicious anemia. Like the latter, it manifests spontaneous remissions and is influenced by intramuscular liver therapy. Dameshek (New Eng. J. Med. *218*: 15-38, 1938) questions whether Wintrobe is justified in believing that these bloods are similar to those of pernicious anemia.

Shumacker and Wintrobe (Bull. Johns Hopkins Hosp. *58*: 343-377, 1936) damaged the livers of dogs, rats and rabbits by the use of carbon tetrachloride. The first response was a more or less marked polycythemia. Later the blood became normal. With an increase in dosage another period of polycythemia was liable to follow. After the period of poisoning had elapsed, the animals had a tendency to become anemic and remain so. The anemia was normocytic at first and later became macrocytic. After damaging the liver of rats with carbon tetrachloride, Higgins and Stasney (Folio haemat. *54*: 129-144, 1936) observed the development of a macrocytic anemia. They believed that there was a definite correlation between the extent of the hepatic cirrhosis, the degree of anemia and the extent of the macrocytosis.

Evidence has been presented showing that an absence of hydrochloric acid may cause hypochromic anemias because iron is not well absorbed if the acid is deficient (Mettier and Minot, Am. J. M. Sc. *181*: 25-36, 1931). Confirming this conception, Kellogg and Mettier (Arch. Int. Med. *58*: 278-284, 1936) report that patients with bleeding ulcers do not recover from their anemia as rapidly on the Sippy regimen as without alkalies. That animals and patients may become anemic following gastrectomy has also been observed, and Kellogg, Mettier and Purviance (J. Clin. Investigation *15*: 241-248, 1936) found that the regenerative power of the hemoglobin was apparently greatly reduced if a gastrectomy had been done on a dog which had previously been rendered anemic by repeated bleeding. Before gastrectomy, the output of hemoglobin averaged 1.59 gm. daily, whereas after operation there was an average output of 0.08 gm. Apparently the animals were unable to obtain, from beef, substances essential for hemoglobin. This suggests that any process depleting the iron stores, such as a deficient diet, prolonged and profuse menses and frequent pregnancies, in a patient with achlorhydria may lead to a hypochromic anemia.

Barer and Fowler (Arch. Int. Med. *59*: 785-792, 1937) found that patients with an achlorhydria retained less iron than did those with a normal gastric acidity. However, the administration of as much as 200 cc. of hydrochloric acid did not increase the retention of iron. If a large amount of iron is given, the presence of an achlorhydria does not appreciably diminish its retention, and the addition of hydrochloric acid under these conditions does not significantly increase the amount retained.

THE INTESTINAL VESSELS

The condition of the blood vessels must exercise a considerable effect on the behavior of a system as vascular as the gastrointestinal tract, and recent studies emphasize the effect of anoxemia on the intestines.

Van Liere and his co-workers (Am. J. Digest. Dis. & Nutrition *3*: 94-97, 1936; Am. J. Physiol. *115*: 239-244, 1936) found that an anoxemia increased the tone of the pyloric sphincter in animals in 14 out of 17 trials. A striking increase in tone occurred when the animals breathed 6 per cent oxygen, equivalent to an altitude of 30,000 feet. After nine minutes the tone fell off toward

normal and the character of the contractions changed. They became less frequent and were quite vigorous and prolonged, approaching a condition of spasm. The contractions assumed their normal character only after the anoxemia had been discontinued for five minutes. With 9 per cent oxygen, corresponding to an altitude of 22,000 feet, there was an immediate and marked rise in the tone of the sphincter, followed by a fall to nearly normal after ten minutes. The antrum of the stomach, however, showed an immediate fall in tone. With 14 per cent oxygen, corresponding to an altitude of 10,000 feet, the tone of the sphincter remained unchanged for three minutes and then rose for an equal period of time. Concurrent with the rise of tone, the frequency of contractions was increased and became more spastic in nature. After six minutes the record assumed a normal character. In another experiment, the authors investigated the absorption of water from the small intestine at the various levels of anoxemia. They found that an oxygen percentage of 15.4 per cent did not effect an appreciable change. With 12.3 per cent there was less absorption than with the controls. With a higher degree of anoxemia there was considerably more absorption. The maximum increase in absorption occurred at 10.6 per cent of oxygen. From then on it decreased.

Van Liere (Arch. Int. Med. *58*: 130-135, 1936) also found that anoxemia affects the emptying time of the human stomach, although there was a considerable individual variation in the response. At a pressure of 560 mm. of mercury, corresponding to 15.3 per cent of oxygen and 8000 feet altitude, 2 or 3 men showed a prolongation in gastric evacuation. The others showed a slight acceleration. The acceleration of the emptying time was noted also when the pressure was at 515 mm. of mercury, equivalent to an altitude of 10,000 feet, although 6 men showed a definite prolongation. At 460 mm. of mercury, corresponding to an altitude of 14,000 feet and an oxygen pressure of 12.3 per cent, each subject showed definite prolongation of gastric evacuation.

Fine et al. (Ann. Surg. *103*: 375-387, 1936) have reported the beneficial effect on gaseous distention of causing patients to breathe a concentrated solution of oxygen. They used a concentration of 95 per cent and reported the effect on 4 cases.

Because the skin and intestinal vessels behave similarly, it seems probable that changing the temperature of the surface of the body will influence the behavior of the intestinal tract. Sleeth and Van Liere (Am. J. Physiol. *118*: 272-275, 1937) have in fact shown that a low outside temperature decreases, while a high outside temperature increases, the emptying time of the stomach.

Booth and Strang (Arch. Int. Med. *57*: 533-543, 1936) have studied the effect of eating on the skin temperature and the blood pressure. Large-sized meals caused a slight rise in blood pressure immediately following the start of the meal, and a return to the previous level followed its completion. The skin temperature, however, showed a rise ten minutes after the beginning of the meal, which continued and amounted to 0.9°C. in twenty-two minutes, when eating stopped. There was a further steady increase to 1.8°C. in forty minutes. The maximum elevation of 2.0°C. was attained at the end of a third twenty-minute period. The rise in obese patients was less marked. This evidence refutes the theory that a person feels chilly after eating because there is a constriction of the skin vessels. A chilly sensation may be due to a more rapid loss of heat because of the dilatation of the surface vessels.

Dunphy (Am. J. M. Sc. *192*: 109-113, 1936) has studied the past history of 12 patients who ultimately died of mesenteric vascular occlusion associated with arteriosclerosis, and found that there was a story of chronic recurrent abdominal pain preceding the fatal attack by weeks, months or years. In 11 of the cases mesenteric arteriosclerosis appeared to be the most plausible cause of the abdominal pain. Seymour and Liebow (Ann. Int. Med. *10*: 1033-1041, 1937) report the symptoms of 5 patients who had narrowing of the celiac and mesenteric arteries. These consisted of upper abdominal pain, sometimes associated with the ingestion of food, abdominal tenderness and, to a lesser degree, distention and a feeling of fullness. Either constipation or diarrhea may be present. The pain was frequently intermittent, analogous to intermittent claudication in the extremities or the angina pectoris which occurs on effort.

Franklin and McLachlin (J. Physiol. *90*: 254-256, 1937) have made the interesting observation that ligation of the mesenteric vein in the cat causes vomiting, whereas ligation of the splenic vein does not.

ESOPHAGUS

Lendrum (Arch. Int. Med. *59*: 474-511, 1937) has made careful anatomical studies of the cardiac orifice of the stomach. He uses the word cardia to cover the area of transition between the histologic structures of the esophagus and the stomach. He studied more than 150 human cardias. In none of the specimens was there seen any special band of circular muscle separated by partitions of connective tissue such as Horton observed at the pylorus. Both circular and longitudinal muscles appeared to be absolutely continuous from the esophagus into the stomach. The author was forced to conclude that in human beings there is no morphological evidence of a sphincteric muscle at the

cardia. From his studies on comparative anatomy, one would not expect an anatomic sphincter at this point.

Some writers believe that cardiospasm is due to a passive process caused by an exceptional amount of elastic tissue, but Lendrum was unable to demonstrate an exceptionally large amount of elastic tissue in this area. He made careful studies on the number of ganglia in the myenteric plexus around the cardia. After developing what he considered a normal finding for this region, he studied the records of 13 patients who died after a so-called cardiospasm. In all these the dilated portion of the esophagus was separated from the stomach by an undilated segment of esophagus. This segment varied in length from 1.5 to 4.5 cm. In no case was there organic narrowing of the neck or scarring around it. This seems to rule out fibrosis of the terminal esophagus as the cause of cardiospasm. The vagus nerve was entirely normal in 10 patients from whom adequate sections could be obtained. However, in every case there was a striking loss or complete absence of the ganglion cells from the myenteric plexus. Occasionally there was actual inflammation in or about the ganglion. This loss of cells was as great in the undilated neck at the cardia as in the dilated portion. Lendrum therefore believes that his results are compatible with the theory that cardiospasm is primarily a disease of the myenteric plexus.

For those who are doing medicolegal work an article by Vinson (Am. J. Digest. Dis. & Nutrition *3*: 457-459, 1936) may be of interest. He reports 4 cases that developed trouble with the esophagus following external trauma. The first patient had been struck with the butt of a gun during bayonet practice. A few days later he had a negative abdominal exploration. Two weeks later he experienced difficulty in swallowing. Ultimately a diagnosis of cardiospasm was made. The second patient vomited blood following abdominal trauma in an automobile accident. Six months later a benign stricture in the lower esophagus was found. The third patient developed her symptoms after injury in a railroad wreck. The fourth patient was struck over the chest in an automobile accident, which caused a rupture of the esophagus 4 cm. long, on the anterior wall.

STOMACH

Physiology

Barron (Am. J. Digest. Dis. & Nutrition *4*: 631-636, 1937) studied the human gastric motor mechanism in patients upon whom bilateral resection of the splanchnic nerves had been done for the treatment of essential hypertension. Balloons were passed into the stomach and the contractions were recorded by the kymographic method. Patients were enabled to register the presence of abdominal distress on the tracings by means of a key magnet. Great variations in gastric activity were noticed; it seemed to be influenced by the state of the gastric tonus which existed at the time of operation. Observations made from eight to ten days after operation, when the results of trauma and anesthesia could be ruled out, revealed very short periods of motility, alternating with short periods of gastric quiescence. After three or four days of this there ensued intense, persistent gastric activity, together with a definite increase in the amplitude of the contractions. Studies made on the emptying time of the stomach showed that there was little or no change after unilateral resection. After bilateral resection, the emptying time was somewhat decreased.

Barron, Curtis and Lauer (Arch. Surg. *35*: 675-693, 1937) have also studied the effect of a laparotomy on the gastric motility. The first effect was an inhibitory one which lasted from twenty-four to seventy-two hours after the operation. This was followed by a period of gastric hypermotility which existed from two to three weeks. During this time the patient might complain of gas pains or a sensation likened to that of intense hunger.

Gershon-Cohen and Shay (Am. J. Digest. Dis. & Nutrition *4*: 637-643, 1937) have shown how increased osmotic tension in the small intestine retards gastric evacuation. A standard meal was fed to patients who normally had only a 10 per cent retention after thirty minutes. An admixture of 20 per cent glucose caused a 50 per cent retention, and 40 per cent glucose caused a residue of 85 per cent. If the glucose was instilled directly into the duodenum, a similar effect resulted.

By making jejunal fistulas in animals and observing the stomach through the fluoroscope, Waugh (Arch. Surg. *33*: 451-466, 1936) was able to introduce solutions into the intestine without interfering with the stomach itself. By this means he has reemphasized the inhibitory effect which fat has on the stomach. When fat was placed in the jejunum, there resulted a marked atony of the whole stomach for periods of from thirty to ninety minutes, during which time there was no sign of peristalsis. If the fat was placed in the stomach the effect was much less pronounced.

Winslow and Herrington (Am. J. Hyg. *23*: 143-156, 1936) have accurately recorded the influence of an odor upon the appetite of 8 young men who were placed in a room, the air of which could be circulated and all climatologic conditions controlled. Studies were made on the appetite when the air was clean and when it contained the odor of house dust. When taking an attractive menu, no difference was observed in the subjects' appetite when

the odor of dust was in the air. With a less attractive menu there was an insignificant decrease in consumption. When the least attractive menu was given, the odor of dust reduced the consumption of food by 13 per cent. Mild odors, in the absence of any great urge to eat, will therefore reduce appetite, although the person eating is not aware of the odor.

Meyer et al. (Am. J. Physiol. *119*: 600-602, 1937) have made a study of the ptyalin content of human saliva in old age. The subjects consisted of 27 persons with an average age of eighty-one and 12 controls with an average age of twenty-five. It was found that the basal saliva of the older group contained 0.30 units of ptyalin per cubic centimeter of saliva. The younger group contained 10.15 units of ptyalin. After stimulation by chewing diabetic gum, the older group showed 0.28 units, whereas the younger group showed 8.20 units. The authors estimated that while 50 gm. of white bread will be digested in the mouth and stomach of young persons, only 1 per cent of this will be digested by older persons. This work parallels the findings on the gastric contents as determined by Alvarez and other workers. It suggests that the secretions of the whole intestinal tract become diminished with advancing age, and is one of the reasons for the increased difficulty in the digestion of older persons.

The gastric secretions have been resubmitted to careful studies by Hollander (Am. J. Digest. Dis. & Nutrition *3*: 428-430, 1936; *3*: 651-655, 1936). By making a pouch of the Pavlov type with an artificial sphincter at the mouth of the pouch, he was able to obtain juices from the parietal portion of the stomach which were freer from contamination by extraneous substances than those previously developed. Under such conditions, the pH of the secreted juices was constant and did not bear any relation to the secretory rate. In other words, the stomach secreted acid at a fixed concentration. Hollander found, as have others, that the neutral chloride varies inversely with the free hydrochloric acid. To test the possibility that the juice with a constant acidity might be a pure secretion of the parietal cells, he extrapolated the neutral chloride in terms of acidity. Thus, the theoretical specimen of gastric juice possessed a neutral chloride value of zero and an acidity of 167 millimols. The gastric juice corresponding to these values is the ideally pure parietal secretion. The constant acidity juices which he had previously obtained represented pure parietal fluid contaminated by small amounts of other secretion from the gastric mucosa. So far there has not been acquired a similar amount of data concerning the other secretions of the stomach, namely those containing organic phosphorus and inorganic phosphates. Figures for these other substances suggest that the stomach may make two secretions, hydrochloric acid and what may be called the buffer secretion, the combination of which produces a fluid isotonic with the blood. On this basis, a decrease in the amount of acid secreted will be balanced by an increase of buffer substances. Therefore, in any sample of mixed gastric juice the sum of the concentrations of the total base and total acid will be equal to the sum of the concentrations of the chloride. Both these sums will be less than the isotonic concentration, about 170 millimols, by an amount equal to the amount of acid lost as carbonic acid or carbon dioxide. In any given sample of gastric juice, the relative values for the concentration of hydrochloric acid and neutral chloride depend on the relative value of parietal and buffer secretions. Hollander believes that this buffering secretion arises as an independent one and does not depend upon mucin.

In general, students have looked for the control of gastric acidity within the gastrointestinal tract itself. It is obvious that there must be some control, and whatever the governing mechanism is, it varies somewhat in different patients. Wide differences occur, and we should do well to speak of an average rather than a normal acidity. Recent experimentation suggests that conditions within the blood exert an effect on the production of hydrochloric acid. Apperly and Crabtree (J. Physiol. *73*: 331-343, 1931) suggested that the plasma bicarbonate was intimately associated with the formation of free hydrochloric acid. This was later confirmed by Browne and Vineberg (J. Physiol. *75*: 345-365, 1932). More recently, Apperly and Cary (Am. J. Digest. Dis. & Nutrition *3*: 466-469, 1936) have demonstrated a striking similarity between the average gastric acidity for different age and sex groups as determined by Van Zandt et al. and the average hemoglobin content of the blood for similar groups from Peter Van Slyke's work. If the figures of these two groups are plotted together a straight-line relation is revealed. These authors have studied the gastric acidity in patients with acute and chronic hemorrhage, and have found that although the acidity varies in different individuals with the same erythrocyte volume, in general the acidity rises in all cases coincident with an increase in the volume of red cells.

Townsend et al. (Am. J. M. Sc. *194*: 636-645, 1937), in a study on the anemia of chronic glomerulonephritis and its relation to gastric acidity, have found that with an increasing anemia there is a decrease in gastric acidity. Furthermore, an absolute achlorhydria develops when the carbon dioxide of the whole blood falls below 30 vol. per cent.

Kiefer (Am. J. Digest. Dis. & Nutrition

4: 667-673, 1937) also studied this problem, and found that an increase in the bicarbonate ion resulted in the displacement of an equivalent amount of chloride. He suggests that this is why alkalies cause an increased secretion of hydrochloric acid. However, he was not able to demonstrate a relation between the elevation of the carbon dioxide of the blood and the gastric secretion. In 7 of the 11 cases there was no corresponding increase in acid secretion after the carbon dioxide was elevated; on the contrary, there was a tendency in the opposite direction. He suggests that this apparent contradiction to Browne and Vineberg's results may be explained by the fact that their work was on dogs, in which the changes in the carbon-dioxide levels are enormously greater than those available in a clinical study.

GASTROSCOPY

Although it is too early to know just how much gastroscopy is going to contribute, it at least supplies a new method of studying the stomach. Since the perfection of the flexible gastroscope by Wolf and Schindler in 1932, gastroscopy can be performed by anyone with a little practice, although much experience will be required before one can be sure of what he observes. Its contraindications are virtually the same as those for the passage of a stomach tube. (Schindler, Am. J. Digest. Dis. & Nutrition *2*: 656-663, 1936; Jackson, Ann. Otol. Rhin. Laryng. *44*: 1150-1156, 1935; Freeman, Am. J. Digest. Dis. & Nutrition *4*: 312-315, 1937; Symonds, Arch. Phys. Therapy *17*: 574-580, 1936.)

Schindler has described the gross anatomy and some physiologic qualities of the stomach as viewed from the inside, as opposed to most of our knowledge, which has been acquired from postmortem and roentgen studies. The so-called "incisura" as seen from within shows a prominence or kind of fold which gives the impression of an angle. It is rare to observe peristaltic waves proximal to this fold. The distal part appears more globular than our usual conception of a tube-like canal, as observed by the x-ray. Peristaltic waves are seen as circular elevations which move to the pylorus and are accompanied by a shortening of the antrum until closure of the pylorus is complete. They are often accompanied by the formation of radial folds, which give the pylorus a stellar appearance. Although it is frequently stated that the stomach is fixed at the cardia and pylorus, gastroscopy shows that although the diaphragmatic portion of the esophagus is fixed, the pylorus is not. Schindler was unable to observe any influence of the abdominal wall upon the stomach.

As a result of gastroscopy, new interest has been awakened in the subject of gastritis. Changes in the mucous membrane may be superficial, in which case the surface epithelium is cloudy and spotted with red in contrast to the normal uniform orange-red. Less often the entire mucous membrane appears purple. Superficial erosions may be present, surrounded by deep, red, hemorrhagic halos. Layers of adherent glairy and white secretion or a gray, dirty, stringy secretion may be present between the folds.

There is an atrophic gastritis in which the mucous membrane becomes gray-green and appears to be thin; the green spots are commonly round or oval. A more marked degree of atrophy may occur, as originally described by Henning. The mucous membrane is grayish pink, gray or grayish green. Heavy, prominent branching blood vessels are seen through the thin mucosa. Small erosions and broad subepithelial hemorrhages may occur.

Hypertrophic gastritis appears to be a swelling of the mucous membrane. The lining appears velvety and flabby. Rigid small folds may occur as well as small warts and nodules. Eventually, gross nodules and tumor-like pseudopolyps develop.

Gastroscopy has contributed little that we did not already know concerning the cause of gastritis or its treatment. However, according to Schindler and Ortmayer (Arch. Int. Med. *57*: 959-978, 1936) superficial gastritis heals completely and does not tend to recur if the patient is treated with rest in bed and a carefully supervised diet. Atrophic gastritis is thought to be an end stage and may remain stationary on proper therapy, but the mucous membrane never becomes normal again. Hypertrophic gastritis lasts for years and rarely develops into an atrophic type. The authors believe that it is impossible to classify the type of gastritis from the symptoms. Patients suffering from superficial or hypertrophic gastritis show a periodicity of distress in a certain proportion of cases. The distress is usually localized in the upper portion of the abdomen, chiefly in the epigastrium, and is reported as a dull, burning or gnawing pain, usually developing one to three hours after eating. About half the patients obtain relief by taking food or alkali. (Schindler, Ortmayer and Renshaw, Arch. Int. Med. *60*: 143-153, 1937.)

It is still too early to know how important gastroscopy is in the diagnosis of such conditions as ulcer and carcinoma. Most gastroscopists believe it to be superior in many cases to the x-ray in differentiating these conditions, and that an occasional lesion can be recognized earlier by this means than by the x-ray. (Schloss, Ettinger and Pratt, Am. J. M. Sc. *193*: 171-180, 1937.) Chevallier

(J. de méd. de Lyon *17*: 719-732, 1936), for example, states that cancer in the antral portion of the stomach can often be recognized by means of the gastroscope when it would otherwise be missed.

Gastric Cancer

Dublin (Am. J. Surg. *31*: 197-203, 1936) states that recorded deaths from cancer of the stomach in the United States for 1932 included 16,000 males and 11,000 females, the accrued death rate being 21.6 per 100,000 population. Duodenal cancer accounted for 1 per cent of the males and 2 per cent of the females. The death rate increased with the years. Between the ages of twenty-five and thirty-four it was 2 per 100,000; between thirty-five and forty-four, 10.8 for males and 7.8 for females; between forty-five and fifty-four 46.7 for males and 30.6 for females; between fifty-four and sixty-four 132.7 for males and 181.1 for females. In recent years the death rate for white males has shown a definite downward trend between the ages of twenty-five and forty-four. There has been virtually no change between forty-five and sixty-four.

Ewing (Am. J. Surg. *31*: 204-205, 1936) discusses the beginnings of gastric cancer, having studied 12 early cases encountered in 10,000 autopsies. In only 1 of these was the diagnosis suspected during life. The study shows that gastric cancer may begin as a localized overgrowth in the mucosa that affects primarily normal cells, which show atypical overnutrition and overgrowth. Infection, erosion and ulceration appear to supervene very early. One case showed erosion of slightly elevated patches in which the glands were distinctly hyperplastic and were beginning to invade the muscularis mucosa. The author believes that this is the mode of origin of many superficial, erosive carcinomas. He emphasizes that this condition does not develop from the chronic hypertrophic form of gastritis, and suggests that it is the result of the local action of some strongly cancerogenic irritant. Furthermore, he points out that since a large proportion of gastric cancers are superficial and merely erosive in the early stages, they will probably not be revealed to the radiologist by any definite tumor. Adenocarcinomas ulcerate early, and the presence of cancer on the edges of an ulcer does not indicate that it is the sequel of the ulcer.

The results of Ewing's study are of course compatible with the well-known clinical fact that by the time a carcinoma can be diagnosed it is usually too late for a cure to be effected. Furthermore, it explains why it is difficult to distinguish by x-ray between an early cancer and nonmalignant variations of the mucosa. It is to be hoped that an improvement in the technical study of the mucosa by the x-ray, together with gastroscopy, may lead to earlier diagnoses of this disease. However, great caution must be exercised in the interpretation of the roentgenographical studies of the mucosa. For example, Rigler (J. A. M. A. *107*: 2025-2028, 1936) reports a case of leukemia of the stomach which on roentgenological examination showed very marked rugae which might be mistaken for so-called hypertrophic gastritis. Under x-ray therapy, the symptoms and the abnormal x-ray appearance entirely subsided. Kantor (Am. J. Roentgenol. *35*: 204-207, 1936), on the contrary, reports 2 cases of localized hypertrophic gastritis which simulated the appearance of carcinoma by x-ray. Since roentgenologists have been carefully reporting the appearance of the gastric mucosa, an increasing number of patients are noted as having hypertrophic gastritis. Clinicians must remember that this form of study is still in its infancy. It was not many years ago that roentgenologists either did not recognize differences in the mucosa or did not consider its appearance. It is often difficult to associate the x-ray reports with the clinical symptoms, and the frequency of the diagnosis leads one to believe a so-called hypertrophic gastritis is often an exaggeration of a normal condition. The two reports just mentioned emphasize the need for caution in accepting such interpretation until more time has elapsed for a better evaluation of the x-ray appearances of the stomach mucosa.

Levin and Kuchur (Lancet *1*: 204-205, 1937) conducted an investigation on 167 relatives of patients with gastric cancer, using as controls the husbands and wives of patients with the disease. They found a high incidence of achlorhydria among the older relatives, not found in the control group. They believe, therefore, that this increased incidence of achlorhydria is further evidence for the idea that cancer is associated with a constitutional type.

Although carcinoma of the duodenum is comparatively uncommon, Castleman (Ann. Surg *103*: 348-352, 1936) points out that under certain conditions the disease is not particularly rare. Of 65 necropsies in which cancer involved the pylorus, 6 showed invasion of the duodenum. From 1919 to 1934, of 134 surgical specimens of the stomach resected for pyloric cancer, 15 showed duodenal extension. In 1934, when special attention was given to this subject, 7 out of 28 surgical cases showed it. Surgeons are urged to resect at least 3 cm. of the duodenum of patients who show a pyloric tumor.

Feyrter (Virchows Arch. f. path. Anat. *295*: 480-501, 1935) reports a neoplasm of the nerve tissue which he encountered in 4 of 2800 autopsies in which the stomach and intestine were carefully examined. It occurred in the cardiac end of the stomach, fundus, jejunum and cecum respectively. Grossly, it is a small, fairly well-circumscribed nodule in the mucosa, not larger than a pea, with

a smooth or finely villous surface. All 4 neoplasms occurred in men from thirty-eight to fifty-eight years of age and were alike in their main features. Histologically they consisted of a network of granular spindle cells in connection with Meissner's plexus, and whereas they may have originated in an overgrowth of Schwann cells, they probably arose from proliferation of some nerve cell, so far unrecognized. The connective-tissue framework contained elements that were indistinguishable from the Gaucher cell.

Peptic Ulcer

Several articles (Tomoda, Arch. f. klin. Chir. *190*: 134-163, 1937; Chang, H., and Chang, F., Chinese M. J. *52*: 143-160, 1937; Chang, C. C., Chinese M. J. *52*: 161-176, 1937) have recently come from the Far East giving statistical data on the incidence and behavior of peptic ulcer in Japan and China. From these accounts it appears that the manifestations of the disease are the same among Orientals as among other peoples. Because the Oriental is supposed to be more phlegmatic and possibly more philosophical than his Western brethren, one would suppose that the incidence of ulcer would be less. However, the Japanese and Chinese must have plenty to worry about at the present time, which may account for the similar incidence of this disease in those nationalities.

Etiology

Although investigative studies continue to emphasize the importance of hydrochloric acid as an etiologic factor in peptic ulcer (Gage, Ochsner and Hosoi, Arch. Surg. *32*: 1019-1048, 1936; Howes, Flood and Mullins, Surg. Gynec. & Obst. *62*: 149-157, 1936), evidence has accumulated to show that the factor which determines whether a patient will have an ulcer depends on the resistance of the mucous membrane to the corrosive effect of the hydrochloric acid. One cannot see large numbers of patients with ulcer without being impressed by the fact that the symptoms tend to come and go without any obvious change in the degree of gastric acidity. However, so far as the reviewer is aware, Brown and Dolkart (Arch. Int. Med. *60*: 680-693, 1937) were the first to make a careful study of this point. These authors studied 20 patients, of whom 15 had a duodenal ulcer and 5 were controls in whom no ulcer could be demonstrated, but who received ulcer therapy similar to that given the patients. These subjects were studied for an average of 150 weeks, and a total of 1036 gastric analyses were performed. During this investigation the authors were able to observe seventy-three recurrences of ulcer activity. Their data demonstrate that the ulcer activity bears no definite relation to the onset of the recurrence. A rise in free acid was observed prior to a reactivity in 46 per cent of the recurrences. In 34 per cent, however, the values for acid were lower than the preceding levels, and in the remainder no significant change in the acidity was observed. In the same patient the level of free acid may rise, fall or undergo no alteration prior to a recurrence. Conversely, there were repeated marked rises in the level of free acid without recurrence. On the other hand, Weech and Paige (Am. J. Path. *13*: 249-256, 1937) show how undernutrition alone may lead to lesions in the stomach. They have been studying nutritional edema in dogs by means of low-protein diets. Of 22 dogs, 12 died spontaneously from severe inanition or terminal infection; 10 were killed by intracardiac injections of ether after extreme inanition had set in. Eight (36 per cent) had developed a true peptic ulcer on the diet. Five (23 per cent) exhibited a superficial erosion of the gastric or duodenal mucosa, leaving 9 (41 per cent) which showed neither ulcer nor erosions. Likewise, Howes and Vivier (Am. J. Path. *12*: 689-700, 1936) discuss the hyperplastic and ulcerative lesions which are so frequently found in the stomachs of rats under abnormal dietary conditions. After their rats had been on a modified Pappenheimer and Lorrimore diet for forty-two days, 9 out of the 10 animals developed lesions in the stomach. In the rumen, the smaller lesions were grossly rounded, ulcerated areas, although the edges were not undermined. The ulcer occurred in hypertrophic squamous epithelium. Animals given the same diet but without cod-liver oil also developed the lesions, but yeast plus cod-liver oil gave complete protection.

In order to decide how justified is the radical treatment of ulcer, it is important to know how serious the disease is. Therefore, Monroe and Emery (New Eng. J. Med. *217*: 729-730, 1937) studied the cause of death in 161 patients previously known to have had an ulcer. Of these, death was due to ulcer in only 54 per cent, the others having died from some unrelated cause. In cases where the location of the lesion was definitely ascertained, the greatest mortality occurred among the gastric, gastric and duodenal, and duodenal ulcers, in the order named. Perforation, hemorrhage and obstruction were the immediate causes of death, in the order named. The death rate so far as could be determined was 6 per cent.

Stalker, Bollman and Mann (Arch. Surg. *35*: 290-308, 1937; Am. J. Digest. Dis. & Nutrition *3*: 822-827, 1937) studied the production of peptic ulcer by cinchophen. They administered the drug by rectum, parenterally, by intestinal fistulas and orally to dogs with fundus pouches, and ulcers devel-

oped in all cases. They concluded that ulcers occur after absorption of the drug and are not the result of the cinchophen's coming in surface contact with the mucous membrane. Histologically and grossly, these ulcers are similar to those occurring in man. The initial destruction occurs in the mucosal cells. The progress and healing are similar to those observed in other experimental ulcers. Mechanical irritation produced by incorporating bones in the diet caused a more rapid development of the ulcers, but did not apparently decrease the rate of healing. In treating these animals, some benefit seemed to come from a diet of milk alone. The use of a duodenal extract appeared to have some prophylactic value. Mucin seemed to be definitely beneficial in certain cases, but in others chronic ulcers developed which were similar to those found in the control animals fed cinchophen without prophylactic treatment. A chronic lesion was not produced in the presence of an alkali-milk diet. No benefit was observed from intramuscular injections of histidine. In none of the animals subjected to gastroenterostomy did gastric, duodenal or jejunal ulcers develop, unless a pyloric or gastric exclusion had been performed. No lesions were observed in an isolated pyloric segment, although definite ulceration occurred when acid-secreting mucosa was included in the isolated portion of the stomach. The authors conclude from these observations that gastric acidity is a factor in the experimental production of peptic ulcer by the administration of cinchophen.

Considerable controversy has arisen concerning the work of Aaron and Weiss on the effect of histidine hydrochloride in the treatment of ulcer. Numerous papers have reported beneficial results in the sense that patients developed early relief from symptoms. The difficulty with many of these reports is that patients have not been studied for a sufficient length of time to determine whether the treatment produces permanent results. The nature of the disease is such that 50 or 60 per cent of patients observed at any one time and under any one treatment may spontaneously become free from symptoms. Hence the efficacy of any treatment can be decided only by observing patients over a period of several years. As time has gone on, it has become evident that histidine treatment has not contributed anything of real value. (Rivers, Am. J. Digest. Dis. & Nutrition *3*: 698-704, 1936; Sandweiss, J. A. M. A. *108*: 700-707, 1937; Sandweiss, Saltzstein and Glazer, Am. J. Digest. Dis. & Nutrition *4*: 20-23, 1937; Wilhelmy and Hashinger, J. Kansas M. Soc. *37*: 45-48, 1936; Feldheim, Presse Méd. *44*: 1189-1191, 1936; Eads, Ann. Int. Med. *10*: 639-644, 1936; Barry and Florey, Lancet *2*: 728-734, 1936; Weigand, Pennsylvania M. J. *39*: 860-863, 1936; Korbsch, Arch. f. Verdauungskr. *59*: 83-103, 1936; Volini and McLaughlin, Illinois M. J. *69*: 39-45, 1936.) It is undoubtedly true that various observers have found that injections seem to cause immediate relief of some patients' symptoms, but it is difficult to rule out the psychologic effect which such a treatment may exert, particularly as every type of hypodermic injection seems to produce the same sort of result (Meriwether and Mitchell, Hosp. News U. S. Public Health Service 2: 8-17, 1935; DiBenedetto, Beretervide and Barrios, Prensa méd. argent. *23*: 1035-1041, 1936). However, when an attempt has been made to control the psychologic influence, as was done by Sandweiss, no benefit could be attributed to the histidine treatment. He treated patients with parenteral injections of histidine, vaccines and other substances. A control group received hypodermic injections of normal saline. From 54 to 66 per cent of patients receiving parenteral injections became symptom-free immediately. At the end of one year the relapses following parenteral treatment varied from 87 to 92 per cent; with diet or surgery it varied from 46 to 54 per cent. The author repeated the work of Weiss and Aaron by treating dogs on which a Mann-Williamson operation had been done with 1 cc. of histidine twice daily, but could not demonstrate any benefit from the drug. Barry and Florey also tested Weiss and Aaron's theory by experiments on cats and pigs. In this case they used the experimental Meckel's diverticulum devised by Matthews and Dragstedt as a basis for testing the efficacy of histidine. Some of the cats were not treated and others were given daily injections. Histidine was incapable of preventing the formation of ulcers when these were caused by the action of unneutralized gastric juices on intestinal mucosa.

There have been no special changes in the surgical treatment of peptic ulcer in the last few years, although there is a tendency to resort to more radical types of operation. Although European surgeons have been doing massive resections for a long time, those in this country have been slow in taking it up. More recently, however, there have been a greater number of reports in the literature on its use. Most of these do not give a long enough follow-up to enable one to determine the value of this type of operation. The operation is possible with a reasonable mortality in the hands of a good technical surgeon, but observations on its effect for periods of four or five years will be needed before one can determine when and in what cases this operation should be attempted. Meanwhile, a word of caution should be interjected. Patients are not so well off without their stomach as with it, and one should hesitate to sub-

ject a patient to this operation without definite evidence that it is his only chance for a reasonably comfortable life.

The use of aluminum hydroxide for the treatment of peptic ulcer in this country goes back to 1929. Since then, several articles have advocated its use. The drug appears to do no harm, and according to Eveleth and Myers (J. Biol. Chem. *113*: 467-471, 1936) it is stored primarily in the liver and spleen and also in the kidneys. After intravenous injections in dogs it appears promptly in the bile and urine. In 1936, Woldman and Rowland (Am. J. Digest. Dis. & Nutrition *2*: 733-736, 1936) suggested letting the material drip into the stomach so that complete and continuous neutralization could be established. A nasal catheter is passed into the stomach and attached to a specially constructed drip bottle. In favor of the treatment is the freedom of danger from alkalosis. Aluminum hydroxide is an amphoteric substance, adsorbing acid in the acid medium of the stomach and giving it up in favor of alkalies when it passes into the duodenum. It is said to have a deterrent effect on the secretion of acid, in addition to the neutralizing value that it possesses. Adams, Einsel and Myers (Am. J. Digest. Dis. & Nutrition *3*: 112-120, 1936) report that there is a definite decrease in the volume of gastric secretion after the administration of colloidal aluminum hydroxide. Studies of the blood did not reveal any decrease in plasma chlorides, even after months of treatment. The highest figure for the carbon-dioxide combining power was 69 vol. per cent. In most instances it did not rise above 60, and at no time did any subject show a value exceeding 70 vol. per cent. No significant deviation from the initial level was found in the total bases of the blood. (Jones, Am. J. Digest. Dis. & Nutrition *4*: 99-102, 1937.)

Ivy and his co-workers (Am. J. Digest. Dis. & Nutrition *3*: 879-883, 1937) studied the effect of aluminum hydroxide on dogs. Contrary to the studies on man, they report that after the administration of aluminum preparations four times daily for as long as four months there was no decrease in the amount of acid secreted; if anything there was a slight increase, which suggests that the stomach attempts to compensate for the buffering action of the aluminum.

Clinicians continue to have diverse views on the best way to treat patients following massive hemorrhages from ulcers. There is no unanimity of opinion on when to transfuse them. Bock (New Eng. J. Med. *215*: 421-425, 1936) believes that a transfusion should be given relatively early. Wood (Brit. M. J. *2*: 115-121, 1936) also argues strongly for early transfusion. He asserts that the recent introduction by Marriott and Kedwick of continuous intravenous blood transfusions has provided a new weapon for the treatment of hemorrhage. When citrated blood is given at the rate of 90 to 150 cc. an hour, the hemoglobin in severely depleted cases is slowly elevated to more than 70 per cent in twelve to forty-eight hours. After the transfusion is finished the hemoglobin sometimes tends to fall, but the drop is insignificant and of short duration. Wood describes a series of cases illustrating changes in mental state, hemoglobin percentage and blood urea. He suggests that the changes in height of the blood urea indicate the extent and rapidity of gastrointestinal hemorrhage and are an aid to prognosis and treatment.

A belief in early transfusion seems to receive support from the evidence of Christiansen that deaths from hemorrhage may result from an azotemia rather than anemia. On the other hand, Alsted (Am. J. M. Sc. *192*: 199-208, 1936), who has made further studies on azotemia following hemorrhage into the digestive tract, could find no relation of the azotemia to the different methods of treatment. Of 25 patients studied, 22 bled from an ulcer, and 3 probably from esophageal varices. Blood-urea values were about 50 mg. per cent in all cases. Alsted could find no relation between the blood-urea values and the percentage of hemoglobin; the increase in blood urea sometimes lasted for days after the hemorrhage. He believes that there may be a functional reduction of renal activity caused by the low blood pressure.

Meulengracht (Wien. klin. Wchnschr. *49*: 1481-1485, 1936) continues to report better results from feeding patients immediately after a hemorrhage than from starvation. Not only is the bleeding thought to stop sooner, but the blood is said to regenerate more quickly. From all the data before us at the moment, it seems probable that there is a distinct advantage in presenting to the body, either by transfusion or natural gastric digestion, certain factors which are necessary to the regeneration of the blood. Unfortunately, however, no statistics have been compiled which permit adequate comparison of all the various methods of treatment. Until such figures become available, physicians will have to rely upon their own experience in choosing the method for treating the individual case.

LIVER

Functional Tests

The search for liver-function tests that will aid in the diagnosis of liver disease still goes on. The problem is a complicated one because the liver has so many functions and because it has such a large factor of safety. The difficulty of these tests is that

a disease process does not influence any one function consistently. White (New Eng. J. Med. *216*: 1017-1023, 1937), in reporting on the galactose tolerance and urobilinogen test in the differential diagnosis of painless jaundice, found that the tests were as a rule positive where diffuse liver-cell damage predominated, as in catarrhal jaundice and toxic hepatitis. In acute infectious hepatitis, 14 out of 17 cases gave a positive urobilinogen test at some period of the disease, and 10 cases had a positive galactose test. In mild cases the tests were not particularly useful. In 4 cases that did not follow the general rule, it was evident that the time of the test in relation to the period of the disease is very important. In 1 case in which there was real difficulty in diagnosis, neither of the two tests gave any help. In 17 cases of toxic hepatitis following drug therapy, the galactose test was positive in all but 2. In other words, the test cannot be considered specific for this disease. In 12 obstructive cases the urobilinogen was almost entirely absent as a result of very little or almost no bile's reaching the bowel, but this observation is not likely to give us any more information than is the test for determining the presence or absence of bile in the intestine. In summary, White points out that the tests were as a rule negative where there was malignant obstruction of the common bile duct. He believes that the combination of these two simple tests has proved a useful aid in distinguishing several groups of medical and surgical cases, namely acute and chronic, toxic and infectious hepatitides and painless obstruction outside the liver. However, the reviewer believes that one cannot ignore the fact that so long as any tests show exceptions to the rule they are not to be relied upon exclusively. Shay and Fieman (Ann. Int. Med. *10*: 1297-1303, 1937) emphasize that to obtain the greatest value from the galactose test it must be applied early in the course of the jaundice. Because of the possibility of some excretion of glucose, it is suggested that differential fermentation of the urine with yeast should be a routine technic in all cases in which the excretion of reducing substances in the five-hour urine exceeds 3 gm.

Flood et al. (Arch. Int. Med. 59: 981-999, 1937) have studied the serum-phosphatase values in 25 cases of obstruction of the extrahepatic biliary tract, 34 cases of catarrhal jaundice, 13 cases of toxic hepatitis, 16 cases of cirrhosis of the liver, 20 cases of neoplasm and 15 miscellaneous cases. Although the phosphatase activity was increased in every case of obstruction of the common bile duct, the results varied widely in catarrhal jaundice and hepatitis. Phosphatase activity was also found to vary over a wide range in cirrhosis of the liver, and exceeded a normal limit of variation in most cases of carcinoma with metastases to the liver. This overlapping between different types of cases was also found by Cantarow and Nelson (Arch. Int. Med. 59: 1045-1050, 1937). Having studied 31 patients with obstruction and 22 with hepatocellular jaundice, the authors conclude that with such a wide overlapping this procedure is of no value in differentiating the two types of jaundice. Rothman and his co-workers (Am. J. M. Sc. *192*: 526-535, 1936) point out that the tests can serve as a means of differentiating the two classes of jaundice only in the absence of other conditions affecting phosphatase. However, they believe the test to be superior to others for differentiating obstructive and non-obstructive jaundice.

Millbourn (Acta chir. Scandinav. 77: 523-562, 1936) has studied the urine diastase values in cases with various disturbances of the liver and bile ducts. He concludes that values of 512 and higher in jaundiced cases in which the diagnosis hangs between stone in the common bile duct, malignant tumor and acute hepatitis are in themselves of certain, though limited, help. Increase in the value of diastase occurs in somewhat more than half of all cases with stones in the common duct and jaundice, in somewhat more than one quarter of all tumor cases with jaundice, and in about one tenth of all hepatitis cases with jaundice. In this test there is no sharp dividing line by which one can make a definite diagnosis. Quick (Arch. Int. Med. 57: 544-556, 1936) reports on the clinical value of the hippuric-acid test in diseases of the liver. He summarizes his observations as follows:

> The existence of hippuric acid after the administration of sodium benzoate was studied on a series of 100 cases in 58 of which hepatic or biliary disease was present. The patient with a normally functioning liver excreted approximately 3 gm. of benzoic acid in the form of hippuric acid, 4 hours after taking 6 gm. of sodium benzoate. A low output of hippuric acid occurred in cases of catarrhal jaundice and various forms of hepatitis, and usually in cases of a malignant process with metastases to the liver, syphilitic cirrhosis and atrophic and hypertrophic cirrhosis. The test is normal in cases of cholecystitis and cholelithiasis and biliary obstruction due to stones in the common duct, if the condition is of short duration. It appears as a promising means for estimating hepatic insufficiency and as an aid in distinguishing between the jaundice of hepatitis and the jaundice arising from obstruction due to stone in the common duct. The test is useful in following the course of disease of the liver and in determining the effectiveness of therapy.

Snell and Plunkett (Am. J. Digest. Dis. & Nutrition 2: 716-721, 1936), after studying the test on a series of 38 patients, concluded that the rate of synthesis of hippuric acid was a reasonably accurate and satisfactory test for the determination of parenchymatous hepatic damage, particularly in

the surgical types of jaundice. The errors noted were no greater than are those to which other hepatic functional tests are subject.

Kirk (J. A. M. A. *107*: 1354-1357, 1936) in a study on 106 patients found the Takata-Ara test to be positive in 80 per cent of the patients with cirrhosis of the liver and in about 50 per cent of those with liver abscess. There were fewer positive results in the following conditions: tumor of the liver, leukemia, hepatitis, passive congestion, tuberculosis, hypertrophy and cholecystitis. The author concludes that the test is not diagnostic for cirrhosis, and is likely to be positive in any disease in which the globulin level is elevated. Magath (Am. J. Digest. Dis. & Nutrition 2: 713-716, 1936), after a study of 86 consecutive cases, concludes that the test will be positive in slightly more than half the patients in whom there is moderately severe damage to the liver parenchyma.

Bollman and Mann (Am. J. Physiol. *116*: 214-224, 1936) have studied the formation and destruction of bile salts by the liver. They produced biliary fistulas and biliary obstruction in some animals and completely removed the liver in others. Normal dogs excreted only traces of bile salts in the urine, and these were not definitely detectable in the normal blood. Only a small amount of the salts injected into the blood appeared in the urine, although the injected material rapidly disappeared from the blood. Sodium glycocol given by mouth did not increase the content of the salts in the urine after their administration to animals on whom complete removal of the liver had been performed. Ninety to 100 per cent was excreted within twelve hours. Subsequent to a ligation of the common bile duct, definite bilirubinemia and bilirubinuria occurred within six hours. Bile salts were evident within twelve to twenty-four hours after operation. Within the next twelve hours there was usually a marked rise in the content of salts in the blood up to 40 or 50 mg. for every 100 cc. of blood. This figure declined in the next two weeks until a level of about 15 or 20 mg. was reached. This level persisted for several months thereafter. Bile salts occurred in the urine during the second twelve hours following operation and increased in amount until a definite level was reached on the third or fourth day after operation. However, injection of bile salts did not give the same quantitative recovery in the urine as occurred after complete removal of the liver. When they were given by mouth there was an increase in urinary elimination, although the total amount excreted by this route was usually less than that given. In hepatic necrosis with complete biliary obstruction there occurred a marked diminution in the urinary excretion of the salts. The authors believe that the liver destroys about half the bile salts which it makes. This study suggests that investigation of the behavior of the bile salts may be of value in studying diseases of the liver and the biliary tract.

Kohlstaedt and Helmer (Am. J. Digest. Dis. & Nutrition *4*: 306-312, 1937), in studying the composition of human fistula bile, found that a marked increase in the concentration of the bile acids followed the oral administration of the salts. The bile volume did not parallel the rate of excretion of bile acids and cholesterol.

McNider has reported a type of simple atrophy occurring in the liver of senile dogs, and has been able to reproduce this change by causing severe hepatic injury. Sprunt (Arch. Path. *24*: 738-742, 1937) in a study of 387 human livers found similar changes in 11. He was unable to establish any correlation with this type of change and the history of the patients.

During the last few years, much good work has been done on the physiology of the common bile duct. Excellent studies have been made on animals, and more recently, clinical studies have been reported on the behavior of the sphincter of Oddi in man.

Walters and his co-workers (J. A. M. A. *109*: 1591-1597, 1937) inserted a T tube in patients who had been subjected to exploration of the common bile duct. After connecting a water manometer to the tube, they observed the intrabiliary pressure which developed and the amount of pressure necessary to overcome the resistance of the sphincter. Morphine and other derivatives of opium, Pantopon, Dilaudid and codeine, distinctly raise the intrabiliary pressure. Amyl nitrite and glyceryl trinitrate definitely decrease it. Intravenous administration of theophylline with ethylenediamine caused relaxation of the sphincteric mechanism. Injection of 0.0009 gm. of atropine failed to cause relaxation, and this was true of 0.0006 gm. of scopolamine hydrobromide. This is the reverse of what Ivy and his workers found in dogs, but may be due to the smaller doses used by Walters. Adrenalin, histamine and alcohol in the doses used did not have any effect on the common bile duct. This was also true of 10 cc. of a 10 per cent solution of calcium chloride. Physostigmine and acetylcholine, which might be expected to increase the pressure, failed to do so. From this data it appears that morphine may precipitate an attack of colic in some patients with lesions of the biliary tract. Ten milligrams of morphine, which does not decrease pain to any extent, may prolong and even augment the increase in pressure in the common bile duct. The pain produced in this way can be relieved by the administration, under the tongue,

of 0.0006 gm. of glyceryl trinitrate or the inhalation of amyl nitrite. Best and Hicken (Surg. Gynec. & Obst. *61*: 721-734, 1935) demonstrated that a disturbance of the sphincter of Oddi can produce pain. By means of direct roentgenographic visualization of the biliary tract they observed an increased spasticity of the sphincter sufficient to produce a mechanical obstruction and to cause retardation of the bile. This spasticity might remain after removal of the gall bladder or of stones.

Surgeons have been advocating dilatation of the sphincter as a routine in gall-bladder operations, with the idea of preventing later symptoms. However, Zollinger and his co-workers (Surg. Gynec. & Obst. *66*: 100-104, 1938) are opposed to dilatation. From a study on dogs and patients they found that spasticity of the sphincter with a resulting dilatation of the common duct was more prone to develop if the sphincter had been dilated. This did not occur if dilatation was not performed.

PANCREAS

The pancreas is one of the very important organs in which it is difficult to determine the presence of abnormalities. It seems probable that Grott (Polska gaz. lek. *16*: 296-300, 1937) is right in saying that many cases of chronic pancreatitis occur which are not apparent and are therefore not diagnosed. Root (J. A. M. A. *108*: 777-780, 1937) has pointed out that acute pancreatitis not infrequently occurs in patients with diabetes, although the diagnosis is not suspected during life. He reports 4 cases occurring in 26 patients who died during or following diabetic coma, an incidence of nearly 15 per cent, and emphasizes that so high an incidence clearly indicates that the diagnosis of acute pancreatitis must always be considered in any case of diabetic coma in which the condition of the patient is extreme and in which proper recovery does not result from adequate treatment for the coma. An analysis of these cases showed that the prostration was more severe than one would expect with a blood pressure of 100 systolic.

It is because of the difficulty of making a diagnosis that so much effort has been expended in study of the pancreatic enzymes. However, the work to date has not been particularly helpful, because the blood diastase rises and remains high for only a few days after an acute obstruction to the pancreatic duct. Thereafter it drops quickly to normal levels. Moreover, there is some question as to whether the enzymes found in the blood and tissues are in fact secreted by the pancreas. Oelgoetz et al. (Am. J. Digest. Dis. & Nutrition *3*: 159-161, 1936) believe that when pancreatic enzymes are given by mouth they are absorbed in the active state, although concentration of the serum enzymes does not increase. They believe that the giving of excessive doses causes that enzyme to be stored in the liver and spleen. Bradley and Belfer (Am. J. Digest. Dis. & Nutrition *3*: 220-223, 1936) are on the other side of the fence. They studied the presence of trypsin in the spleens and livers of hogs. Pancreatic tissue digested more rapidly in an alkaline medium, and the rate of digestion decreased as the medium became acidified. However, when the liver and spleen were studied under identical conditions, there was a barely detectable digestion in the presence of an alkaline reaction. On the other hand, if pancreatic tissue was added to these organs, digestion occurred rapidly under alkaline conditions. This evidence contradicts the theory that trypsin is absorbed from the intestinal tract to be distributed and fixed by the tissues for their metabolic use. The authors state that any system of physiology, pathology or therapy based on the assumption that pancreatic enzymes are regularly present in tissues such as the liver and spleen should be accepted with caution until some competent evidence to substantiate it is forthcoming.

Ivy (Am. J. Digest. Dis. & Nutrition *3*: 677-682, 1936) emphasizes the value of the serum phosphatase in differentiating concomitant obstruction of the liver and the pancreas. Serum phosphatase is usually very high in obstructive jaundice and is also elevated in catarrhal jaundice. However, ligation of the pancreatic ducts causes only a slight temporary rise. Thus it is possible to diagnose acute involvement of the pancreas in the presence of obstructive jaundice. If serum amylase, lipase and phosphatase are all high, the liver and pancreas are both obstructed. If the phosphatase is very high and the amylase and lipase only slightly elevated, the liver is involved and the pancreas is only slightly involved, if at all. If the serum amylase and lipase are high and the phosphatase low, the pancreas is more acutely involved than the liver.

SMALL INTESTINE

Various observers have continued physiological studies on the small intestine of human beings by means of the multiple-lumened tube designed several years ago by Miller and Abbott (Miller and Karr, Am. J. Roentgenol. *35*: 300-305, 1936; Abbott and Pendergrass, Am. J. Roentgenol. *35*: 289-299, 1936; Groen, J. Clin. Investigation *16*: 245-255, 1937; Owles, Clin. Sc. *3*: 1-7, 11-20, and 21-36, 1937). By a combined use of the tube and the x-ray, Abbott and Pendergrass have been able to distinguish between peristaltic-wave contractions and segmental contractions which occur in

the intestine. When morphine was injected it became evident that there was an association between peristalsis and tonus. When the intestine was atonic it was rather inactive. As the tone increased, peristaltic waves became deeper, and then smaller when the rise in tone became marked. Two minutes after the injection of morphine, an abrupt tonic contraction of the duodenum occurred, and nearly obliterated the lumen for twenty minutes. This primary contraction was followed by dilatation, which was often present for three hours. With the marked rise in tonus, all waves, peristaltic and segmental, disappeared. If the pressure in the balloon was raised, small rhythmic waves appeared. As the marked tonus decreased, the amplitude of the contractions increased. It was found that the tonus level in the ileum was more stable than in the upper part of the intestinal tract. No immediate effect occurred in the ileum, and only a slight rise in tonus took place, reaching its height fifteen minutes later. The stomach emptied slowly at first owing to the increased tone, but emptied rapidly as the tone decreased. The general effect of morphine was to cause a rapid downward flow of the duodenal and jejunal contents, which then slowed up, resulting in marked prolongation in the emptying time of the small intestine. Because of this, the authors believe that morphine has a bad effect on patients with distention.

Other studies on motility were made by injecting a dye into a fasting stomach and observing the rate at which it could be removed from the jejunum. This varied from 30 to 100 cc. per hour. Studies on the reaction of the intestinal contents confirm what has been made out by other methods of study, namely, that the average pH is around 5.43 for the duodenum, 6.33 for the jejunum, 6.71 for the upper ileum and 7.30 for the lower ileum.

Using the same type of apparatus, Groen studied the absorption of hexoses in the upper intestine for a distance of 50 cm. He injected 100 cc. of solutions containing varying amounts of hexoses and then thoroughly washed out the loop after one-half hour. He found that there was an increase in the rate of absorption with an increase in the concentration of solution up to 10 per cent. Above this concentration, the quantity of glucose absorbed was independent of the amount introduced. He calculated that 50 cm. of the human intestine absorbed from 10 to 11 gm. of glucose per hour. By keeping constant the absorption time and the quantity of glucose injected, he found that within the limits of experimental error a direct proportional relation existed between the length of the intestine and the quantity of glucose absorbed. Galactose was absorbed somewhat more rapidly than glucose. The absorption rate of levulose appeared to be constant for solutions with a concentration above 6 per cent, and that of levulose was definitely slower than that of glucose and galactose. Studies on the osmotic tension which developed in the injected solution led the author to conclude that the hypertonic glucose solution was diluted until the concentration of the glucose plus the concentration of other constituents in the intestine made an isotonic solution. The author discusses his results in relation to the study of others and suggests that the absorption of sugar occurs at a slower rate in human beings than in rats and dogs.

COLON

The intestinal flora is a source of never-ending interest to the physician. From time immemorial, the thought of autointoxication has been uppermost in the minds of the laity and of physicians. Yet the problem has been so complex that it is fair to say that little advance has been made in this subject. As far back as the end of the last century, Strassburger and Schmidt studied a clinical condition characterized by an apparent intolerance for carbohydrates. From time to time, students have attempted to determine the conditions underlying this interesting clinical state. It was Strassburger's belief that an intestinal catarrh caused an inadequate digestion of starches. The excess of starches which reached the colon then fermented. He believed that if these patients were starved of carbohydrates for ten days or two weeks the organisms feeding on the excess starch would die and the patient would be relieved of his disturbance. Yet the problem of whether the flora is conditioned by the intestinal contents or in some way influences the digestion of the foodstuffs has continued to bother students.

More recently, Gunnison, Althausen and Marshall (Arch. Int. Med. 57:106-116, 1936) have reinvestigated this point, particularly to determine whether it might be due to excessive numbers of *Clostridium welchii,* as stated by Herter and Kendall. They were able to show that there was no correlation between the number of Welch bacilli and the presence or absence of carbohydrate intolerance. They state that rapid fermentation as a guide to the presence of large numbers of fermenting organisms is a fallacy, because an inoculum of only a few organisms can produce maximum fermentation, if conditions chance to be such that multiplication occurs. They were unable to confirm the statements of Kendall and others that aciduric organisms suppress the growth and activity of *C. welchii* in the intestine. There are always a large number of proteolytic organisms, regardless of the character of the aerobic flora, and therefore the aciduric bacteria probably have no

practical effect in suppressing the growth of the former. They conclude that in the present state of our knowledge the clinical laboratory can be of little or no assistance in the diagnosis of so-called carbohydrate intolerance and similar disturbances.

Further to complicate this subject has come the highly interesting observation that the flora is apparently influenced by the mineral content in the diet. Eppright, Valley and Smith (J. Bact. *34*: 81-97, 1937) have shown that the fecal aciduric organisms of rats practically disappear within two weeks after the administration of a low-salt diet, and are replaced by colon bacilli and enterococci. Giving a complete salt mixture caused a marked preponderance of aciduric organisms and a concomitant loss of the putrefactive type. A combination of calcium and phosphorus in the diet produced a marked predominance of aciduric organisms. However, neither of these salts alone produced an aciduric flora. This may explain why milk increases the acidophilus organisms in the intestine. Weinstein and Weiss (J. Infect. Dis. *60*: 1-5, 1937) have shown that banana powder, apple powder and raisins fed to white rats subsisting on a high-protein diet cause a change in the intestinal flora from one in which non-aciduric bacteria predominate to one in which *Bacillus acidophilus* is the main organism. Prunes, charcoal and kaolin do not seem to affect the intestinal flora of white rats. The explanation for the action of banana, apple and raisins is not apparent, but they believe that the carbohydrate and mineral contents of these fruits are of prime importance in their ability to establish an intestinal flora rich in *B. acidophilus*.

Johnson (J. Clin. Investigation *16*: 223-230, 1937) studied the absorption and excretion of calcium and phosphorus in 3 patients with colostomies and ileostomies. In 1 case the amount of ileal elimination varied directly with the quantity of water and food ingested. Increasing the intake of water from a minimum of 750 cc. raised the average ileal elimination from 228 to 322 gm. per day. When viosterol was given a diuresis occurred, with a decrease in the wet ileal elimination from 423 to 370 gm. There was also some decrease in the dry weight, namely from 30.8 to 28.8 gm. Giving 40 units of parathormone caused an even greater decrease in the ileal elimination, namely from 423 to 229 gm. The dry weight dropped from 30.8 to 25.5 gm. The ileal discharges were acid at all times, but were somewhat more so when the patient was fasting than after the ingestion of food. This is a surprising observation because most research suggests that the lower intestine is alkaline when empty. After meals the discharges were about neutral. Washings obtained from the colon contained only a few milligrams of calcium and phosphorus. Raising the intake of these substances increased their elimination. The giving of viosterol did not change the excretion of calcium and phosphorus from the ileum. After the use of parathormone there was a decrease in calcium from 0.6 to 0.5 gm. per day.

Because writers have emphasized the importance of the intestinal tract on the metabolic utilization of minerals, the work of Welch, Adams and Wakefield (J. Clin. Investigation *16*: 161-168, 1937) on the composition of the feces in chronic ulcerative colitis is of interest. There was a relative increase in the fecal excretion of sodium, and consequently its urinary excretion was relatively low in all cases. The distribution of its total output in the urine and feces was abnormal because of the large fecal elimination. The greater amount of fecal potassium was thought to be the result of the increase in desquamated epithelium. Studies of the plasma indicated that the continuous loss of intestinal minerals resulted in a low concentration of sodium and chloride in the blood. As might be expected, the daily weight of the feces was excessive. These patients excreted amounts of nitrogen far in excess of normal, largely in the form of blood and pus. In general, they conclude that there is relatively little if any loss of food in a case of ulcerative colitis, whereas the loss of minerals is large. The study indicates that the colon exerts an important function in the absorption of minerals.

Various investigations of the physiology of the colon tend to confirm the clinical impressions which one receives in watching patients (Bargen and Dixon, Rev. Gastroenterol. *3*: 205-218, 1936). Slive and Fogelsen (Am. J. Digest. Dis. & Nutrition *4*: 17-19, 1937) suggest that the gastrocolic reflex is a misnomer and should be spoken of as an appetite reflex. By introducing a balloon into the colon at various levels through fistulas in dogs, they found that if food was introduced through a stomach tube no peristalsis occurred, whereas eating caused a marked increase in its rate. However, it must be remembered that dogs do not enjoy stomach tubes, and that these animals may have suffered from a psychic inhibition. They add that, if food could be introduced so that digestion would occur immediately, evidence of a gastrocolic reflex might be obtained. Yet there may be a chemical factor associated in the so-called gastrocolic reflex, as opposed to the usual conception of a nerve-transmitting reflex. By studying the colons of animals after various operative procedures, Bargen has shown that an increased secretion of mucus results from irritation of the colon by various

cathartics and that an increased secretion occurs with an increase in its activity. He has also found that when absorption of material from the colon is increased a decrease in mucus occurs, which suggests to him that mucus may in some way act as a regulator of absorption.

It is commonly known that the act of defecation raises blood pressure and that persons may develop a cerebral hemorrhage when straining at stool. Therefore, Klinefelter (Am. J. Digest. Dis. & Nutrition *4*: 12-13, 1937) has studied the effect which defecation has on the blood pressure. He found that there is an average increase in systolic pressure of 20 mm. of mercury and in diastolic pressure of 15 mm. In one patient this effort produced an increase amounting to 100 mm. systolic and 88 mm. diastolic. There was some evidence that the average increase depended, at least to some degree, on the general condition of the patient. Ordinarily one thinks of defecation as a voluntary act, yet Barclay and Franklin (J. Physiol. *90*: 478-481, 1937), when investigating the reflexes on the bladder and large intestine, discovered that if digital compression of the bladder or of the large intestine was performed, and particularly if there was a passage of feces into the rectum, there resulted a marked reflex contraction of the diaphragm and abdominal muscles. This suggests that the act of defecation is purely an involuntary affair after the proper stimulus has been applied.

Sperling (Arch. Surg. *32*: 22-48, 1936) reinvestigated the role of the ileocecal sphincter. Studies were made to determine the pressure which occurred clinically in the colon and to find whether the ileocecal valve was competent to withstand these pressures. He concludes that the ileocecal sphincter can withstand a pressure of from 10 to 50 cm. of water, which is within the physiologic limits of the pressure within the intestine. He points out that if an obstruction of the colon appears distal to the sphincter, the intestine may become altered into a closed loop by the obstruction at the distal end and by the competent ileocecal sphincter at the proximal end of the loop. This change, in turn, may produce all the inherent dangers of strangulation as a result of the increased intestinal pressure affecting the circulation. Sperling states that if a pressure of this degree is produced experimentally in dogs there develop areas of hemorrhagic necrosis in the colon.

DIARRHEA

Because diarrhea is the result of so many causes and because most of them respond readily to the simpler forms of treatment, there is a tendency, particularly in northern climates, not to investigate them thoroughly enough. Few patients are studied from the bacteriological angle. The work of McGinnes, McLean, Spindle and Maxcy (Am. J. Hyg. *24*: 552-567, 1936) is therefore of interest because it throws light on the frequency of the dysenteries and shows the importance of finding the organism in the stools. These workers carried out a study in Henrico County, Virginia, over a period of three years, during which 178 cases of diarrhea or dysentery were reported by physicians. A field nurse obtained knowledge of 124 cases, making a total of 302 cases, in 176 families. Complete records were obtained on 295 cases. Forty-eight per cent of the patients were classed as having dysentery and 52 per cent as having diarrhea. These classifications were based on the clinical behavior of the disease. Dysentery bacilli were isolated from 69.5 per cent of the dysentery patients and 40.9 per cent of those having diarrhea. In each of the clinical groups, approximately two thirds of the positive cultures were of the Flexner type and one third of the Sonne type. Of course the importance of these results depends upon the accuracy with which the observers could make a clinical differentiation between the symptoms of dysentery and those of an ordinary diarrhea. However, of 625 family contacts, 110 were found to be carrying dysentery bacilli at one time or another. In families where 1 or more of the cases were positive, 35.3 per cent of the well contacts carried dysentery bacilli. In families where only 1 case was proved to have bacillary dysentery, 9.3 per cent were found to be carriers. According to the authors, these figures imply that the presence of dysentery bacilli does not necessarily cause the disease and that their presence in a patient having diarrhea does not prove that he is suffering from bacillary dysentery. From a study of the New Jersey epidemic of bacillary dysentery, Felsen (Am. J. Path. *12*: 395-404, 1936) believes that the changes which occur in the intestine depend largely on the selective action of the particular dysentery toxin and the degree of naturally acquired immunity which the patient possesses. The earliest intestinal lesion was found to be a diffuse hyperemia of the mucosa of the small and large intestines with moderate edema and diffuse lymphoid hyperplasia of the solitary lymph nodes. The latter stood out as grayish, punctated, rounded elevations. Sections at this stage revealed hyperplasia of the lymph nodes, edema of the submucosa and a marked dilatation of all the superficial vessels. Glandular cells secreted large amounts of mucus. The inflammation became more intense on the second or third day and fresh blood began to ooze from the surface. Superficial ulceration was frequently followed by hemorrhage. The lymph nodes became larger and underwent a central ne-

crosis. The average case did not go beyond this stage, reached its peak in one week and entirely cleared up in about three weeks. Many cases were characterized from the start by an acute inflammation of the terminal ileum. In the Jersey City epidemic 122 out of 210 hospitalized cases were re-examined nine to twelve months after the acute attack. Of these, 19 per cent gave definite clinical roentgenographical evidence of chronic ulcerative colitis. This is of considerable interest because there are many observers who believe that nonspecific ulcerative colitis may start as a bacillary dysentery and then fail to heal completely. Thus, Winkelstein and Herschberger (Am. J. Digest. Dis. & Nutrition 2:408-411, 1935) report the presence of dysentery bacilli in 7 of 60 cases with chronic ulcerative colitis, and state that positive agglutination tests for the dysentery organisms occurred with the serums from 22 per cent of their series.

Chronic idiopathic ulcerative colitis still remains idiopathic. Paulson (J. A. M. A. *109*: 1880-1886, 1937; Am. J. Digest. Dis. & Nutrition *3*: 667-673, 1936) has been working on the theory that the disease is caused by a virus. Grumbach and Haemmerli (Arch. f. Verdauungskr. 59: 239-266, 1936) studied the streptococci isolated from cases with chronic ulcerative colitis, and concluded that there was no evidence that the disease was caused by a specific organism.

Bargen and Barker (Arch. Int. Med. *58*: 17-31, 1936), as a result of observing thromboses in 18 patients out of about 1500, emphasize that extensive arterial and venous thromboses may be serious complications in chronic ulcerative colitis. They reported 6 cases. All the patients were young adults between the ages of nineteen and thirty-one, had been in bed for several days or weeks, and had marked secondary anemia. All the cases were of the severe type of colitis, with fever and evidence of toxemia. Perforation of the colon occurred in 2 cases.

319 Longwood Avenue.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 24281

PRESENTATION OF CASE

First admission. A sixty-eight-year-old white, Canadian woman entered the hospital with the complaint of jaundice of four days' duration.

About six months before entry she began to lose weight, although she had a good appetite and felt well. Her weight fell from 170 to 126 lb. at the time of entry. Two weeks before entry her appetite began to fail, and she ate little except milk and fruit. Her stools became clay colored, and her urine dark. However, there was no change in her bowel habits. Eight days before entry she began to have dull, epigastric pain, which radiated to the middle of her back between the shoulder blades. The attacks occurred about once a day, often at night, lasted fifteen to twenty minutes and were relieved by gaseous eructation. Four days before entry she noticed that her skin was yellow. The jaundice gradually deepened, but the pain became less severe.

In her youth she had had typhoid fever, but had never before had jaundice. For four or five years she had had epigastric distress after meals, relieved by soda, but she had never had persistent nausea and vomiting, hematemesis, melena or other gastrointestinal symptoms. Her past history was otherwise negative, and her family history was noncontributory.

Physical examination revealed a well-developed woman who showed evidence of considerable weight loss. There was marked jaundice of the skin and mucous membranes. The heart and lungs were negative. The blood pressure was 120 systolic, 80 diastolic. The liver edge was palpable. There was no spasm or tenderness. The pelvic and rectal examinations were negative.

The temperature was 98.6°F., the pulse 90. The respirations were 25.

The urine contained a slight trace of albumin, 2+ bile and occasional casts. The blood showed a red-cell count of 4,500,000 with 80 per cent hemoglobin, and a white-cell count of 7400 with 67 per cent polymorphonuclears. Five stool examinations were guaiac negative. The blood Hinton and Wassermann tests were positive. The icteric index was 75, and the van den Bergh 29.5 mg. per cent, direct. The bleeding and clotting times were normal, and the corrected sedimentation rate was 0.45 mm. per minute. A gastrointestinal x-ray series showed no definite evidence of organic disease of the esophagus, stomach or duodenum. The gall bladder, however, was very much dilated and contained many calculi.

On the seventh day a laparotomy was performed. A small, shriveled gall bladder containing stones was removed, and several stones were scooped out of the lower end of the common duct. She had a somewhat stormy convalescence; but her jaundice and other symptoms disappeared, and she was discharged six weeks after operation.

Second admission (six months later). In view of her age she was not given antisyphilitic therapy, and she was well until two days before re-entry. At that time she developed erysipelas of the face. The disease ran a nine-day course, and she was discharged cured. Her liver was slightly tender and palpable 3 cm. below the costal margin. The blood Hinton and Wassermann tests were still positive.

Third admission (thirteen months later). Her general health remained very good and she was readmitted for treatment of bleeding varicose ulcers of the left leg. The liver edge was not palpable at that time. Ligations and injections of the saphenous veins were done, and she was discharged improved after six days.

Final admission (twenty months later, about four years after her first admission). She felt well until about one year before re-entry, when she began to notice very gradual increase in the girth of her abdomen. However, she had no particular symptoms and was able to lead an active life. Two weeks before re-entry she developed rhinitis, with a productive cough and slight sore throat. She stayed in bed because of malaise, which persisted up to the time of re-entry. She had no other symptoms except inconstant, stabbing pain in the left lower quadrant. On the night of admission she suddenly vomited about 500 cc. of dark-red liquid blood. She had no nausea or abdominal pain and did not perspire or go into collapse. She fell asleep almost immediately.

Physical examination revealed a pale, chronically ill woman, lying flat in bed. The skin showed a vague lemon-yellow tint, and there were ecchymoses over the left eye and on the left arm and legs. The heart and lungs were negative. The blood pressure was 100 systolic, 60 diastolic. The abdomen was distended, and there was dullness in the left flank, although no definite fluid wave could be made out. The liver edge could not be felt. A few external hemorrhoids were present, and there was minimal edema of the ankles.

On pelvic examination the cervix was pulled upward and was not freely movable. The fundus of the uterus could not be outlined.

The temperature was 99°F., the pulse 100. The respirations were 24.

The urine examination was negative. The blood showed a red-cell count of 2,500,000 with 35 per cent hemoglobin, and a white-cell count of 8000 with 75 per cent polymorphonuclears. The stool gave a 4+ guaiac test.

She was reasonably comfortable until fifteen hours after admission, when she again vomited bright-red blood and simultaneously passed dark-red liquid blood by rectum. The melena and hematemesis continued, and she died three hours later.

Differential Diagnosis

Dr. John H. Talbott: This woman was sixty-eight years old when she was first seen in this hospital. Five years before she had had a gastrointestinal upset. Her weight decreased from 170 to 126 lb. in six months. With this striking loss of weight in such a short time in a patient over sixty, one of the first things to consider is cancer. The history of epigastric distress, relieved by soda, and the radiation of the pain are characteristic of gall stones. Pain at night is also characteristic. She had had typhoid fever when she was a child, and we know that the incidence of gall stones following this disease is high.

On physical examination the only thing of importance is the large liver, which was palpated 5 cm. below the costal margin. It was not tender, however, and there was no evidence of tenderness over the gall bladder, and no spasm. The stools were examined for guaiac-positive material. Presumably malignant disease was seriously considered. She had positive Hinton and Wassermann tests. The sedimentation rate was slightly elevated.

A laparotomy was done, and I presume the preoperative diagnosis was carcinoma of the pancreas. I should like to know whether we have any description of the organs at operation.

Dr. Tracy B. Mallory: The preoperative diagnosis was carcinoma of the head of the pancreas. A stone was found in the common duct, and it and the gall bladder were removed.

Dr. Talbott: Apparently they made a thorough examination of the pancreas and stomach and found no evidence of malignancy; at least no mention is made of it.

Dr. Mallory: Nothing was found.

Dr. Talbott: The patient had a stormy convalescence, partly, I presume, due to her age. She was a chronically ill person who had lost a great deal of weight, and had been sick for some time, with stones in the common duct. I think it was a credit to the surgical service that she recovered and went home. Then she had erysipelas. We see this frequently in people who are chronically ill, and her recovery — probably before the days of sulfanilamide — is a credit to the medical service. At that time the liver seemed to be smaller than it was on the first admission. If we can place any reliance on the statement that it was 5 cm. below the costal margin on the first admission and only 3 cm. on the second admission, we can say the liver was shrinking in size. On this admission we again have positive Hinton and Wassermann tests.

At the third admission, thirteen months after the second, the liver was not palpable. I do not see how we can get away from the fact that the liver was definitely shrinking in size. I cannot believe it was all due to the position of the patient or of the diaphragm.

She had been quite well until a year before her last admission, when she noticed increase in the size of her abdomen. If she had had this increase for a period of a year, it is strange that they could not be certain of a fluid wave or fluid in the abdomen, provided it was due to abdominal ascites. She developed cough and slight sore throat and had pain in the left lower quadrant. On physical examination they found something not noted at the first admission. The cervix was pulled upward and was not freely movable. The fundus of the uterus could not be outlined. Again one must not be hasty and say that she did not have cancer. I do not believe she had cancer of the pancreas. There is little evidence to suggest that she had pelvic cancer. This change of findings in the pelvis cannot be satisfactorily explained by the clinical diagnosis which I propose to submit. She had pain in the chest, and the question of whether she had small pulmonary infarcts might be raised. She had a faint lemon-yellow tint to the skin. In cirrhosis, when it is difficult to be certain about the presence or absence of jaundice, the term subicteric is applied. Such a term is appropriate as many times there is only a minimal elevation of bilirubin. The blood pressure was down. She was in slight shock, although at the time of the first attack of vomiting she had not gone into collapse. There was edema of the ankles, and little else except fatal hemorrhage.

In the history we have the positive Hinton and Wassermann tests staring us in the face. If this were a syphilitic hepatitis it would be unusual to have the first symptoms at the age of sixty-six or seven. She had something going on during the year before admission which was responsible

for her loss of weight. This process I do not believe was malignant disease. It had been going on for at least a year before admission. She had had a laparotomy and lived for four years. She died not from something associated with the laparotomy but from hemorrhage. We should have more evidence than we have if she had a carcinomatous lesion. I think the changing size of the liver is significant. Whether she had a so-called toxic hepatitis at the time of first admission, which was responsible for the jaundice, and whether the acute episode was simply the passage of stones, I do not know. I am more inclined to accept than reject it. She had some symptoms which suggest pulmonary infarct. She had pain in the left lower quadrant, which could be accounted for by a venous thrombosis. If she had something in the abdomen going on for a year, let us say ascites, and had hepatitis, general venous thrombosis is a possibility.

My final diagnosis is a toxic hepatitis which was followed by cirrhosis with esophageal varices; she probably had thrombosis of the splenic veins which may have been partly responsible for the development of the varices and the terminal hemorrhage. She had serological syphilis. I have been trying to make a diagnosis of syphilitic hepatitis for a long time, and if this patient were fifteen years younger, I should make it here. I cannot believe this is syphilitic hepatitis, however, in view of the fact that the first symptom appeared at the age of sixty-six.

Dr. George W. Holmes: It would have been interesting to have had a careful study of the esophagus for varices. It may have been done, but I do not see any report. There is no enlargement of the heart, and so far as I can see, the stomach is normal. There is a very large gall bladder filled with stones, and a defect in the duodenal cap. We have films of the chest — one taken at full inspiration and one at expiration. It is interesting that her heart is not enlarged or abnormal in shape and that she shows only a moderate amount of arteriosclerosis, with no evidence of dilatation of the aorta, which is somewhat against syphilis. In the film taken of the abdomen you can see the kidney outlines quite distinctly on both sides. They are not abnormal in size or shape. She has not small contracted kidneys or anything that would lead one to suspect renal disease. The liver edge is in about the normal position. There is a shadow above the left kidney which could be spleen. I should not say that it was a normal spleen, for as a rule we do not see the spleen.

Dr. James H. Means: The source of the hematemesis is of interest. I recall a patient we discussed here, a man somewhere near this patient's age, on whom we made a diagnosis of cirrhosis of the liver. He had hematemesis and we supposed it came from varices, but the x-ray people could not demonstrate any varices. He later came to autopsy, and it turned out that he did have cirrhosis of the liver but also a peptic ulcer which was the source of the hemorrhage. It is too bad that we have no picture of the esophagus.

Dr. Wyman Richardson: I have made the diagnosis of cirrhosis of the liver many times and have usually been wrong. I am going to bet on it again — portal cirrhosis.

Dr. Walter Bauer: This woman was interesting for many reasons. She tolerated morphine much better than the average patient with cirrhosis of the liver. Given in full doses it did not produce a state of coma, although such has been reported. She was of further interest because she had considerable true pitting edema of the abdominal wall. It was probably a manifestation of her low serum protein which, if I remember correctly, was about 4.6 gm. per cent. The edema of the abdominal wall was so marked that if she lay on her side for some time the edema fluid would gravitate and thus give her abdomen, when she later lay flat on her back, the appearance of a boat turned upside down; then, when the edema fluid had again gravitated, her abdomen took on the contour of one containing a large amount of fluid. We thought that she had cirrhosis of the liver and that she was bleeding from esophageal varices. The reason I thought so was that she had a very suggestive color, although she did not have what we commonly speak of as a cirrhotic facies. She did have purpura, ascites, and extremely severe uncontrolled hemorrhage, which of course was responsible for her exitus.

Dr. Mallory: I was rather hoping that some one would raise the question of biliary cirrhosis. In a patient with gall-bladder disease, with stones in the common duct and with the etiology for prolonged obstruction in the other ducts, that would be the most usual type of cirrhosis to expect. Of course there are many points against it, particularly this rapid progressive shrinkage of the liver. The liver must have been very large on the first entry and atrophic at the fourth entry.

Clinical Diagnosis

Chronic hepatitis with ascites and ruptured esophageal varices.

Dr. Talbott's Diagnoses

Toxic hepatitis (first admission).
Cirrhosis of liver (idiopathic).
Hemorrhage, ruptured esophageal varix.
Thrombosis of splenic veins.
Syphilis (serological).

Anatomical Diagnoses

Cirrhosis of liver (? alcoholic).
Rupture of esophageal varices.
Ascites.
Healed rheumatic endocarditis, mitral valve.
Operative wound: cholecystectomy.

Pathological Discussion

Dr. Mallory: The autopsy showed a markedly atrophic cirrhosis of the type that one could call portal. The spleen was not so much enlarged as I should have expected, or as it probably was during life. It weighed only 180 gm. It was soft, shrunken and wrinkled, and unquestionably, the terminal hemorrhage must have bled out the spleen and caused it to shrink a great deal in size during the last few hours of life. No thrombi were found in the splenic vein or portal system. The esophagus showed varices which we were able to make out after a little difficulty. We did not find the actual site of rupture, but at any rate there was no ulcer from which she could have bled. The kidneys showed a moderately advanced state of vascular nephritis. As to what the etiology of the cirrhosis is, I am completely in the dark. I should have said from the gross appearance that it was alcoholic: it was small and finely granular. However, such a diagnosis appears to be ruled out by the history.

Dr. Bauer: She denied the use of alcohol, but it was interesting that she cried after the question was asked.

Dr. Mallory: One has to realize that in the face of overwhelming circumstantial evidence women will sometimes refuse to admit alcoholism.

Dr. Bauer: The way she answered the question was a very good indication that she had consumed alcohol in the past.

Dr. Mallory: I cannot find microscopically any so-called alcoholic hyalin; but she did not have acutely progressive cirrhosis at the time of death. Here is one case in which we can be reasonably sure the cirrhosis was not due to arsenic treatment because she had had none.

A Physician: There was no other evidence of syphilis?

Dr. Mallory: No.

CASE 24282

Presentation of Case

First Admission. A seventeen-year-old, white, American wood chopper entered the hospital with the complaint of cramplike pain in the abdomen.

Two days before entry he began to have cramplike pain in the abdomen, centered around the umbilicus. Several hours later he vomited and continued to vomit all food eaten up to the time of entry. The pain persisted but shifted somewhat to involve the whole lower abdomen and particularly the right lower quadrant. However, the pain ceased a few hours before entry. He was given two cathartic pills by his mother and several other pills for his bowels by his physician. He had had about ten bowel movements during his illness.

One year before entry he had had an attack of lower abdominal pain not accompanied by vomiting which lasted for about three days. His past history was otherwise negative, and his family history was noncontributory.

Physical examination revealed a well-developed and nourished young man apparently acutely ill. The heart and lungs were negative. The abdomen was doughy, and there was moderate generalized tenderness, most marked just to the left and below the umbilicus. There was a considerable amount of voluntary spasm, with some involuntary spasm, most marked in the right lower quadrant. No masses were felt. There was generalized tenderness on rectal examination.

The temperature was 100°F., the pulse 108. The respirations were 20.

The urine examination was negative. The blood showed a white-cell count of 16,000.

A laparotomy was performed immediately, and a ruptured gangrenous appendix was removed. There was a localized peritonitis around the tip of the cecum. The incision was closed leaving one wick for drainage. His convalescence was uneventful for the first eight days. His temperature fell to normal, and there was only slight drainage from the wick. On the ninth postoperative day he began to vomit and continued to do so for three days, when he began to complain of upper abdominal pain. His temperature remained normal, although his white count rose to 25,800. His abdomen was soft and not obviously distended. However, a second laparotomy was performed. Several loops of small bowel were enormously distended, and there was a small amount of free fluid in the abdominal cavity. There were adhesions around the draining sinus, and a loop of the small bowel was twisted upon itself. Most of the adhesions were cut, and the volvulus was straightened out, allowing free flow of intestinal contents into the collapsed distal loops of bowel. A Witzel enterostomy was done before closing the wound. He had a stormy convalescence complicated by stitch abscesses and an urticarial skin eruption but was finally discharged on the thirty-ninth day, four weeks after his second operation.

Final Admission (thirteen years later). During

the next two years he had intermittent attacks of abdominal pain, often with vomiting and other signs and symptoms of intestinal obstruction. He was admitted to the hospital on six occasions, and during two of these, laparotomies were performed for lysis of adhesions. On the other occasions the attacks subsided spontaneously.

Five days before his last re-entry he began to have cramplike pains centered in the lower abdomen, soon followed by nausea and vomiting. The pain was intermittent but gradually increased in severity. On the day of entry his vomitus became dark brown in color and had a definite fecal odor. He had had a normal bowel movement on each day of his illness. He had had no chills, fever, jaundice, hematemesis or melena.

Physical examination revealed a well-developed and nourished man showing considerable dehydration. The heart and lungs were negative. The blood pressure was 140 systolic, 80 diastolic. Irregular intestinal outlines could be seen and felt on the abdominal wall. The abdomen was distended and tympanitic. There were generalized tenderness and resistance throughout, and no peristalsis could be seen or heard. Rectal examination showed high bilateral tenderness.

The temperature was 99°F., the pulse 80. The respirations were 20.

The urine examination was negative. The blood showed a red-cell count of 5,140,000 with 111 per cent hemoglobin, and a white-cell count of 12,600. The blood nonprotein nitrogen was 57 mg., and the protein 7.0 gm. per cent. The carbon-dioxide combining power was 53.2 vol. per cent, and the chlorides were equivalent to 100 cc. of N/10 sodium chloride. An x-ray of the abdomen showed marked generalized dilatation of the small bowel. There was a calcified lymph node in the right side of the abdomen.

A laparotomy was performed on the day after entry. Practically the entire jejunum was markedly distended, and at the distal end of the distended loops there was a violin-string band which passed over the bowel and obstructed it. Adjacent to this band were several adhesive scars running along the mesentery. After lysis of the adhesions, air and fluid passed readily into the collapsed portion of the intestine. An enterostomy was not done. He was put on Wangensteen suction, and for the first postoperative day his general condition was good, although his temperature rose to 101°F. On the second day, however, he began to have a profuse watery diarrhea which continued unchecked for the next three days. During that period he was given two transfusions totaling 900 cc. and four intravenous clyses totaling 11,500 cc. Fluids were also forced by mouth, and it was thought that a positive fluid balance was maintained. His urinary output varied between 800 and 1100 cc. daily. However, his blood pressure fell steadily to 45 systolic, 0 diastolic. He had no abdominal distention, but peristalsis was weak and often not audible. Wangensteen suction was continued. On the fourth postoperative day the blood nonprotein nitrogen had risen to 115 mg.; the serum protein was 5.3 mg. per cent, the carbon-dioxide combining power 51 vol. per cent, and the chlorides equivalent to 94 cc. of N/10 sodium chloride. The rise of temperature to 101°F. on the first postoperative day was maintained. Two days later it rose to 103°F., and then fell to normal on the following day. He died quietly on the fifth postoperative day, with a terminal rise in temperature to 103.5°F.

Differential Diagnosis

Dr. John D. Stewart: A word of comment on this history at the start is worthwhile because of the typical picture which it gives us of acute appendicitis with perforation. A young man is suddenly seized with abdominal pain which is at first generalized, and then shifts to the lower abdomen; the cessation of pain accompanying perforation is then noted. Even the purgation is, unfortunately, not an atypical feature of the story. The course continues to run in a rather familiar way with the appearance of postoperative intestinal obstruction, which not infrequently occurs after drainage of an appendix abscess, being due to inflammatory adhesions. This complication should especially be kept in mind when the abscess lies near the midline, or when there is little omentum to protect the coils of small intestine from the drainage wicks. Apparently the initial attack of intestinal obstruction was successfully dealt with, but later the picture is again definitely that of small-bowel obstruction. The statement that the cramplike pains were centered in the lower abdomen is of interest, for it supplies evidence against obstruction of the small bowel, the pain of which is usually centered in the upper abdomen or midabdomen. We are told that the patient had a normal bowel movement on the day of admission. In incomplete small-bowel obstruction there may continue to be rectal discharges. These can hardly be characterized as normal movements, however, for they are usually watery or scanty.

The x-ray picture of the abdomen is frequently of diagnostic help in acute intestinal obstruction, for it may show a latticework consisting of distended loops of bowel. Layers of fluid and air can often be demonstrated, especially if the picture is made in the lateral or sitting position.

Dr. George W. Holmes: I think we are quite safe in saying that this is small bowel, not large,

and that the obstruction is low in the pelvis. I should not use the term generalized in describing it, although it is not exactly local. There is no evidence of herniation or intussusception. But these possibilities cannot be ruled out without a barium enema.

DR. STEWART: Was this made lying down?

DR. HOLMES: Yes.

DR. STEWART: The blood changes at the time of the first admission are consistent with the examiner's impression of dehydration. In the presence of circumstances which tend to produce dehydration, elevation of nonprotein nitrogen is one of the earliest measurable changes in the blood. The nonprotein nitrogen was elevated here to 57 mg. per cent. The serum protein figure was 7.0 gm. per cent, which is normal. We do not know, of course, what the particular normal level for this patient was. It may have been lower than 7.0 gm. per cent, so that the reading may still represent some concentration of the plasma colloids. Dehydration may occur without disturbance of the acid-base balance, or with alkalosis or acidosis. In this case there is, at the time of the last admission, no demonstrable disturbance of acid-base balance. Typically, in pyloric obstruction we see dehydration with alkalosis. Commonly, in small bowel obstruction we find dehydration with acidosis, but the picture varies from case to case.

"A laparotomy was performed on the day after entry." One might raise the eyebrows a bit at that. Presumably the patient was being prepared for surgical treatment during the interval. Of course the diagnosis of acute intestinal obstruction is an urgent indication for operation, particularly if there is malodorous vomiting, as in this case.

"Fluids were also forced by mouth and it was *thought* that a positive fluid balance was maintained." This is well put, because on the evidence we have here it is difficult to say whether a positive balance was maintained. We do not know how much fluid the patient was losing in diarrheal movements, or through the skin and lungs, or how much was lost as exudate in the peritoneal cavity at the site of the lesion, or how much had been excreted into functionless loops of small intestine.

"Wangensteen suction was continued." At this point I should like to interrupt to insert a word of caution on the use of this measure. The device is capable of doing a great deal of harm unless carefully used. It may be just as dangerous to institute such decompression drainage of the upper gastrointestinal tract as to give a large dose of morphine in the presence of lesions of uncertain type and extent. Mechanical relief results, and alleviation of reflex disturbances, which may mask diagnostic and prognostic evidence until it is too late to start proper treatment of the primary lesion.

A PHYSICIAN: What is the method?

DR. STEWART: A small-caliber tube is passed through the nose into the stomach or duodenum, and is connected with gravity suction bottles. Huge quantities of intestinal and gastric contents can be drained away effortlessly with the device, and the patient may rapidly become dehydrated and depleted, unless adequate replacement fluid therapy is maintained. The method should preferably be used where the diagnosis is perfectly plain and only as a temporary measure.

Of course, the real question in this case is, Why did the patient die? The operation note assures us that there was effective relief of the obstruction. Resection of the intestine was apparently not considered to be indicated, so it is perhaps fair to assume that the viability of the obstructed intestine was not in question. Nevertheless, after a five-day gradual downhill course the patient died. An interesting point is the depression of blood pressure, and I should like to ask how long the hypotension lasted before death.

DR. FIORINDO A. SIMEONE: Two days.

DR. STEWART: Another feature which interests me very much is the blood-chemistry picture before death. Of course, in a terminal state almost any combination of chemical data can be obtained, but assuming that these figures are significant there has been a reduction in the serum protein from the preoperative level of 7.0 gm. to 5.3 gm. per cent. There has been a rise of nonprotein nitrogen to 115 mg. per cent. There is still no particular alteration, so far as we can tell, in acid-base balance. The findings in the blood at this time could be the result of dilution by intravenous fluids. On the other hand, the urinary output had remained low, certainly at an inadequate figure. Bearing on the question of elevation of nonprotein nitrogen in the blood, a good deal of interest has been recently stimulated in the syndrome of so-called uremia secondary to hemorrhage into the gastrointestinal tract. One might take issue with the expressed views on the subject, but Christiansen* has gone as far as to say that in cases of peptic ulcer with severe bleeding into the gastrointestinal tract the fatal outcome may be dependent on uremia rather than blood loss. Another writer has suggested that elevation of the nonprotein nitrogen of the blood may be used as diagnostic evidence of hemorrhage into the gastrointestinal tract.

Were these diarrheal movements bloody?

*Christiansen, T.: Hyperazotaemia in intraintestinal haemorrhage. Acta med. Scandinav., supp. 78, pp. 894-899, 1936.

DR. SIMEONE: No.

DR. STEWART: Was the red-blood-cell count in the terminal period significantly reduced?

DR. SIMEONE: No.

DR. STEWART: I do not know why this patient failed to respond to treatment. All I can say is that he had small-bowel obstruction, that he was severely dehydrated at the time of admission to the hospital, and that he had persistent hypotension, the cause of which is not apparent. I suppose one would have to consider changes in the adrenals, possibly from hemorrhage into them, and changes in the autonomic nervous system incident to a retroperitoneal inflammatory lesion. I do not believe he died of generalized peritonitis, although there may have been local peritoneal reaction at the site of the damaged intestine.

DR. SIMEONE: This man came into the Emergency Ward with obvious acute obstruction and dehydration. According to the record he was operated on the next day, which, to be sure, is correct, but he came in at 11:30 at night and was operated on at 12:30 the next morning — one hour later. I have nothing to add to the operative note except that the adhesion was a band that obstructed the lumen, starting on one side of the mesentery and looping over the intestine to attach to the other side of the mesentery. As soon as the band and adhesions were severed there was free passage of gas through the obstruction. The lumen readily admitted the index finger. The dilated loops of intestine were slightly congested but not infarcted. There was no gross evidence of impairment of circulation in these loops. The collapsed portion of ileum was entirely normal. Postoperatively we tried to get as much fluid into this man as was thought safe. He received from 4000 to 8500 cc. of fluid intravenously per day, besides what he took by mouth, not all of which was removed by Wangensteen suction. In spite of the continued large amounts of intravenous fluid he never showed any edema. The urine remained concentrated and scanty. As Dr. Stewart has said, we do not know exactly how much fluid he lost through his diarrhea but it must have been considerable. His hypotension was probably secondary to dehydration and depletion of the blood volume, leading to circulatory failure.

CLINICAL DIAGNOSES

Intestinal obstruction.
Renal failure.

DR. STEWART'S DIAGNOSES

Acute small-bowel obstruction from adhesions.
Dehydration.

ANATOMICAL DIAGNOSES

(Intestinal obstruction.)
Acute diphtheritic enteritis.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This is the type of case that demonstrates rather vividly the inadequacy of pathologic anatomy. We cannot add much more as to why this man died. The obstruction had apparently been satisfactorily relieved. We did find one anatomic lesion not suspected during life. That was a severe diphtheritic enteritis of that portion of the small bowel which was previously dilated and lay above the point of obstruction. The bowel at the time of autopsy was very dusky in color and strongly suggested a mesenteric thrombosis, but very careful search of the mesenteric vessels, both arteries and veins, showed only fluid blood in all of them. Certainly there was no mechanical obstruction to the circulation, unless it occurred temporarily in the wall of the gut itself from the very severe distention. That is conceivable. The kidneys seemed to be somewhat large, weighing 450 gm., and at the time we thought we might be able to make a diagnosis of nephrosis from microscopical examination, since we have had two other cases in which we found a rather characteristic change in the renal tubules secondary to prolonged, severe dehydration. I cannot recognize such a lesion in this case, however.

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THE APPRAISAL OF MALNUTRITION

It is no news to the physician to realize his own fallibility; more often is it difficult for the layman to appreciate the fact that medicine is not an exact science. During the War a good deal of valuable information was derived from mass statistics, but then, as always, about the most valuable knowledge gained came from the debunking of false concepts.

We knew more about a good many things twenty years ago than we do today. The superiority of our present knowledge lies in knowing that what we knew then is false. One of the hardest but one of the most necessary features of our never-ending education in a rapidly progressing art-science such as medicine is the constant unlearning today of what was yesterday considered as fact.

We have, for a long time, talked and written rather glibly of malnutrition, especially so since the relatively young specialty of pediatrics began to direct more attention to the infant and child. White House conferences were called; children's charters were drawn up; and the nutritional status of the child became a matter of national interest, if not of concern.

It was not until we had had economic depression with us for some time that we began to be concerned in a large way with the possibility of widespread malnutrition, and set about the business of finding out to what an extent this might exist. The problem was tougher than we had anticipated, for it soon became apparent that no two experts, without collusion, could agree upon the biologic facts in question. Malnutrition, in short, was not standardized.

Some of the data obtained have been put together and recently published by the United States Public Health Service.* In one study conducted in New York, six experienced pediatricians examined independently a group of one hundred and eight eleven-year-old boys, and rated their nutritional condition. One physician found fifteen of the group to be malnourished, another only two, and the other four selected twelve, ten, seven and six respectively. To make matters worse, they did not even pick the same children; in fact, only one child was selected by all six examiners.

Similarly, in a school in New Jersey, one hundred and thirteen girls were examined independently by five women physicians. In this experiment there was much more uniformity in the proportion of children found in the poorly nourished group, the actual numbers recorded ranging from twenty-six to thirty-two. The lack of agreement in the ratings of individual cases, however, was even more striking than in the first group. Sixty-five children were found to be malnourished by at least one examiner; there were only six, however, on whom all agreed.

In his summary, Dr. Mayhew Derryberry, Senior Public Health Statistician, who collected the data, suggests that practical nutritional programs be focused on correcting the faulty food habits of children rather than expending energy on routine examinations to determine nutritional status.

*Derryberry, M.: Reliability of medical judgments on malnutrition. Pub. Health Rep. 53:263-268, 1938.

SIR JAMES CRICHTON-BROWNE (1841-1938)

THE recent death of Sir James Crichton-Browne at the remarkable age of ninety-seven recalls a life of noteworthy accomplishment. Browne, born in Dumfries, Scotland, in 1841, obtained his medical degree at the University of Edinburgh in 1868 and, following a brief period of study at the University of Paris, became medical superintendent of the West Riding Lunatic Asylum, Wakefield, England, at the age of thirty. A year or two before, this institution, fortunately near Leeds, had had a brief awakening, from the point of view of medical research, in the activities of Dr. T. Clifford Allbutt, who had begun to use the ophthalmoscope in the wards of this hospital and whose remarkable book, *On the Use of the Ophthalmoscope in Diseases of the Nervous System and of the Kidneys,* was to be published shortly. Rapidly organizing his staff, Browne, in the next six years, supervised sixty-two pieces of research at the hospital, all of which found publication in the *West Riding Lunatic Asylum Medical Reports,* 1871-1876. In addition, the six volumes contain two papers written by men who addressed the medical staff of the hospital and sixteen papers contributed by outside workers. For this brief period of time, there have been few examples in the history of medicine of so much original research's having been carried on under one man's auspices and in a single hospital. It is a great tribute to Browne that he, in an obscure institution for the chronic mentally ill, should have stimulated so much work, all of high quality. He recognized at the very start, and so states in the preface to Volume 1, that public opinion implied at the time that no scientific work could be accomplished in a public asylum and that even if work were done, it failed, as a rule, to achieve any useful result. He succeeded in disproving both of these statements in a manner which, as we look back upon it sixty years later, can only fill us with admiration.

Of all the work done at the asylum, none was more outstanding than the physiological experiments of David Ferrier. He came up from London and was given the resources of the pathological laboratory, with a liberal supply of animals. The object of his research was to put to experimental proof J. Hughlings Jackson's views on the pathology of epilepsy and to augment the studies of Fritsch and Hitzig, who had stimulated the anterior part of the brain with galvanism and noted movement on the opposite side of the body. Ferrier, using faradism, was able to map out in cats and dogs the cortical areas for the face, eyes and extremities and showed, for the first time, that both sides of the brain were symmetrical. He also demonstrated the motor function of the corpus striatum and showed that the thalamus was a sensory organ. Jackson's views on epilepsy were confirmed and, as Sherrington has pointed out, Ferrier gave "localisation of cerebral function a solid basis of proved experimental fact." Prior to Ferrier's time "the cerebral cortex was pictured as an uncharted sea of featurless uniformity." Ferrier's work, although epoch-making, was received with much reserve. It was not until the International Medical Congress of 1881 in London that his demonstrations were fully accepted by Charcot and others.

Browne left the West Riding Lunatic Asylum in 1875, when he accepted the position of Lord Chancellor's Visitor in Lunacy, an important post previously held by J. C. Bucknill. In 1878 he assisted Bucknill, Ferrier and Jackson in founding the neurological journal, *Brain.* The rest of the life of Crichton-Browne (for he so called himself thereafter) is not without interest. He became an important figure in the London medical world, and his advice was widely sought on matters pertaining to the care of the mentally sick. As years went by, he felt less and less the correctness of Osler's dictum that the best work of the world is accomplished by men under forty. In 1905 he wrote an essay attempting to overthrow Osler's point of view. Although Crichton-Browne lived to be nearly one hundred years of age and was a man of great vigor in the last fifty years of his life, one cannot help but feel that his real work was accomplished at the asylum before he reached the age of thirty-five, and that the inspiration he gave to the men under his supervision, which resulted in the large amount of research appearing in the *Medical Reports,* marks an accomplishment in his life which he never even approached in later years.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY

RAYMOND S. TITUS, M.D., *Secretary*
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CASE HISTORY No. 80. BLEEDING BEFORE VIABILITY, TREATED CONSERVATIVELY

Mrs. A. H., a thirty-seven-year-old para II, when approximately twenty-three to twenty-four weeks pregnant, telephoned that she had begun to bleed and was bleeding very freely. When seen at home, she was not flowing, although there was evidence that she had been bleeding. The uterus was soft, the fetal heart heard, and the pulse rate 90. She was put to bed.

The family history was negative. She had had measles and whooping cough as a child; her past history was otherwise negative. Catamenia began at fourteen, were regular, with a twenty-eight-day cycle, and lasted four days without pain. Her last period began February 1, making her due for delivery November 8.

She flowed some more the next day and was advised to go to the hospital, since the amount of bleeding was very material.

Upon entrance to the hospital the uterus was not contracting; it was soft and relaxed. The fetal heart was heard. The fundus was 23 cm. above the symphysis. The blood pressure was 110 systolic, 66 diastolic. She was kept in bed two weeks before a vaginal examination was done, and during that time there was practically no bleeding. The examination revealed no abnormality except a scar in the right vault; the placenta was not felt, and there was no evidence of a varicose vein's having ruptured. Iron therapy (20 gr. of Ferrosate daily) and an anemia diet were prescribed. She was kept in bed in the hospital about six weeks, at the end of which time she was allowed to go home by ambulance, with instructions to remain in bed. She was not allowed up until after the thirty-sixth week of her pregnancy. There was no bleeding after the initial episode.

A blood examination on the day of entry to the hospital showed a red-cell count of 3,700,000 with 68 per cent hemoglobin (Sahli); four days later it was 3,800,000 with 71 per cent hemoglobin, and the day before she went home it was 4,200,000 with 84 per cent hemoglobin.

On November 11 she was delivered by simple forceps of a baby weighing 10 lb., 5 oz., after a short labor. The placenta showed a definite area of degeneration and scar formation near the membranes where it must have separated in part at the time of the bleeding early in her pregnancy. A blood examination showed a red-cell count of 4,800,000 with 90 per cent hemoglobin (Sahli).

Comment. The blood examination on arrival established the real extent of the bleeding, and the case shows the results that can be obtained with rest in bed, iron therapy and an anemia diet.

Conservatism in these cases is always worth while. If the bleeding continues, operation must be entertained, but if it ceases and the patient can be kept quiet in bed, one may expect a successful termination of pregnancy.

A series of selected case histories by members of the section will be published weekly.

Comments and questions by subscribers are solicited and will be discussed by members of the section.

DEATHS

CAHILL — THOMAS J. CAHILL, M.D., of 156 Line Street, Cambridge, died July 4. He was in his fifty-fifth year.

Dr. Cahill received his degree from the Tufts College Medical School in 1907. For twenty years he was chief obstetrician at the Cambridge Hospital.

He was a fellow of the American Medical Association and the Massachusetts Medical Society.

His widow and four sisters survive him.

HOWARD — ALONZO G. HOWARD, M.D., of 56 Bellevue Street, Roxbury, died July 4 at the Massachusetts Memorial Hospitals. He was in his seventieth year.

Born in LaValle, Wisconsin, in 1869, he was graduated from Boston University School of Medicine in 1895 and later became recognized as an expert in orthopedic and fracture surgery. Dr. Howard was professor emeritus of orthopedic and fracture surgery at Boston University School of Medicine, and developed the department devoted to these specialties at the Massachusetts Memorial Hospitals.

He held fellowships in the American Medical Association and the Massachusetts Medical Society and was a member of the American Academy of Orthopedic Surgeons and the American College of Surgeons.

MISCELLANY

PSYCHOLOGICAL ASPECTS OF TUBERCULOSIS

Vis medicatrix naturae is the only hope of the tuberculous patient. The "cure" consists essentially in maintaining as nearly as possible an optimum physiological balance. This balance is a delicate one, easily disturbed by emotions. The very knowledge that one has tuberculosis is, itself, a powerful depressant. Numerous worries, doubts and fears come to plague the patient in his long uphill struggle with this chronic disease. Therefore, the psychologic aspects of tuberculosis play an important part in the treatment. Mary B. Eyre, recovered patient, nurse and psychologist, writes (Public Health Nursing *30:* 279-282, 1938) on this subject to nurses. Excerpts of her article should be of interest also to physicians.

Being able to say, "I had tuberculosis for four years and recovered" aided the author in securing the con-

fidence of patients in a large tuberculosis sanatorium. The purpose of her investigation was to discover what mental hygiene and psychology had to offer in speeding the recovery of tuberculous patients.

The condition of the tuberculous person is one primarily of loss of equilibrium — first of his body chemistry, and then of his family situation, his job and his whole mental attitude. A financial problem is almost inevitably present. All the patient's human relationships are shifted. The husband or wife, the parent or child, the lover or the beloved, the friend, the business associate, the employer or his subordinates — all take on a different aspect. The patient must think differently not only of them, but of himself. He must literally make himself over.

This can happen only gradually, through the continued responses made to the new situation. Our personalities cannot be changed overnight, but they are built up by using our various abilities, just as muscles are developed through exercise. The abilities are ours by inheritance, but what we do with them is our own responsibility. No magical power from the outside can do for a man what he himself must bring about. Psychology can help him to learn how this "will to live," as William James once called it, can be used to help and not to hinder.

Emotion, as the word implies, is a moving force. Energy in the organism means increased metabolism and discharge of nervous impulses. Emotional states lead to activity of the organism somewhere, either externally or internally. If activity of the body be curtailed as in tuberculosis, energy is discharged in worry, fretting and anxiety.

The apparent well-being which so often accompanies tuberculosis is frequently a cloak for hidden fear; exaggerated cheerfulness may be a compensatory mechanism. Probe beneath the gay and hopeful exterior of the tuberculous person and one may find submerged feelings of dread and despair.

The answer to the emotional problem is, in brief, first to recognize the emotional source or cause of the disturbance, and then to use the released energy in some way which will bring full satisfaction. For the tuberculous patient, achievement is far more difficult than it is for the healthy individual. He is, moreover, denied the ordinary relief of moving from place to place, with its variation of social contacts, and the help of a change of occupation by which pent-up restless feelings may be worked off.

All of us need some central stabilizing influence to which we can refer the meaning of our lives. Religion is such a stabilizer, and its therapeutic influence should be utilized.

Psychology must do more for the solving of life's problems than to offer a stone in place of bread. Psychology is valuable in understanding emotions and how to deal with them. One of the most potent emotions is fear. Its results may be seen clinically, as for example in restlessness, loss of sleep, dilated pupils, disturbed digestion, secretory changes, and even, in some cases, increased blood pressure and temperature. It has been shown that the bodily effects of fear and rage involve increased activity of some of the endocrine glands, which in turn are innervated by the sympathetic division of the autonomic nervous system.

A practical way of aiding persons who are emotionally disturbed is to let them talk freely to someone they trust. "Well, how are you today?" cheerfully uttered by the busy doctor or nurse without pausing, will not invite the patient to unburden his deepest anxieties.

When tuberculosis attacks the adolescent there is added reason for fortifying him with clear thinking, sympathetic understanding and intellectual honesty.

During the years of adolescence the psychological strains of living increase, along with the social responsibilities incident to growing up. The boy or girl becomes self-conscious, not only by being easily embarrassed (which is the sense in which the term is most often used), but by the new feeling of "selfness" which begins to appear in the average child at about the age of twelve, together with the ability to deal with abstractions as well as with concrete objects. He becomes capable of regarding himself as apart from the surroundings which he has hitherto accepted without question. He can and often does challenge the established order beginning with home and parents and extending to the entire universe. This is a heady brew for the youngster, and in some instances it aggravates the emotional conflicts which awakening sex life have introduced, until a veritable inner chaos is the result.

The person with tuberculosis must learn not only to control his emotions, but to use emotional energy constructively. Psychology teaches that instead of negation and denial, we should use redirection of energy, and re-education of the individual. — Reprinted from *Tuberculosis Abstracts:* July, 1938.

AMERICAN MEDICAL ASSOCIATION DEDICATES EXHIBIT AT SAN FRANCISCO FAIR

A Western drive by the medical profession against quackery, medical frauds, superstition, malpractice and medical ignorance was launched by members of the American Medical Association at the dedication of the Hall of Science at the 1939 Golden Gate International Exposition on San Francisco Bay. The exhibit sponsored by the American Medical Association was dedicated the same day.

Meanwhile it was announced that the first exhibit to be moved to Treasure Island will be the University of California's $200,000 medical and scientific display, which will be housed in the Hall of Science. Many exhibit pieces, under construction on the campus, are being moved to the great island hall.

Chairman at the dedication was Dr. Ray Lyman Wilbur, president of Stanford University and one-time president of the American Medical Association. Principal speakers included Dr. Irvin Abell, president of the American Medical Association; Dr. Morris Fishbein, editor of the *Journal of the American Medical Association,* and Dr. Thomas Parran, Jr., Surgeon-General of the United States and director of the United States Public Health Service.

CORRESPONDENCE

WHAT THE HOSPITAL OWES THE COMMUNITY

To the Editor: The community has the right to expect that its hospital will maintain the highest possible professional standards. As a guardian of community health, and often supported largely by public funds, the hospital is virtually in a fiduciary position and obligated to maintain such standards which are, in the last analysis, the patient's primary safeguard. The hospital should be in a position to offer the best of care and treatment, and in those cases that require specialized attention not generally available, should be ready to guide the patient properly.

The community, in turn, should not only give financial support both public and private, but moral support through insistence on high-grade personnel with appointments

always on an ability and merit basis. Political influence and favoritism have no place in a community hospital.

We wonder whether trustees and staff men realize how greatly consultants can contribute toward this end.

At the Burbank Hospital we have long been fortunate in having certain outstanding men on our consulting staff who have taken a deep interest in the welfare and professional standards of the hospital, and who have played an active part and given generously of their time and effort. To what extent such assistance, advice and support can assure the success of work in hospitals outside a metropolitan area is being more and more realized and valued. Their regular visits and the modern up-to-the-minute procedures which they suggest or initiate have a most stimulating effect on all groups — physicians, interns, nurses. The entire morale goes forward. Their presentation of important subjects at staff meetings shows what these meetings can be.

Late in 1936 a plan was arranged on the surgical service that brought to us the best leadership in thought, technic and skill, from one of the Boston medical centers. It holds much promise for future surgery at the Burbank Hospital, and if availed of to the fullest extent and as unselfishly as the spirit in which it is provided, the benefits will be very great.

This plan was made possible when the trustees appointed a consulting and directing surgeon, and a consultant and director of bone and joint surgery. They also appointed a consulting and directing physician.

The consulting and directing surgeon has worked with three senior surgeons who have been in charge of and have guided the three-month services. They, in turn, chose four assistants from a group of ten assistant surgeons. In the selection of these four younger men for intensive training, no consideration was given to seniority.

Attempts have been made by the surgical director to assist the latter in difficult and unusual operations, and to observe them and advise them in the management of the ordinary or routine procedures of surgery. It is the belief of the director that, at least for some time, the more major problems in abdominal surgery should not be attempted by the junior men. Only as their training and experience develops and advances shall they advance into the more complicated fields of abdominal surgery.

It is, however, most important that these men should be trained in the routine and fundamentals of surgery, and in the management of the most common surgical lesions of the abdomen. As an example of the success with which this is being accomplished we may say that, over a period of eighteen months, there have been one hundred and fifty-two operations for appendicitis on the ward service, and there have been no deaths. Inasmuch as these patients included those who had perforated appendices with and without local and generalized peritonitis, we feel that the record can well be considered satisfactory evidence of our accomplishment.

Many things go into the reduction of mortality and the improvement of results on a surgical service. Not the least — in fact perhaps the most important — of these is the immediate care of the patient before operation, and the management of the patient after operation. We have made tremendous advances in the last year, we believe, in the preoperative and postoperative management of surgical cases. Except in emergencies all the patients are thoroughly and carefully investigated and studied for several days before operation. In their postoperative period, with the new system of fluid administration and the development of simplified methods of blood transfusion, many otherwise hopeless patients have been carried through to successful recovery.

We have had no hesitation in transferring from our surgical service in the hospital certain cases which we felt would be benefited by the unusual advantages of other institutions. Certain surgical diseases occurring in infants we have transferred to Boston hospitals. Certain very difficult operations on the thyroid gland, stomach and large intestine have also been sent to Boston hospitals. As we develop and improve we may well not have to transfer these patients, but for the moment the best thing for the patient, in our opinion, is to be certain that he has the specialized attention he needs.

We have the pleasure and satisfaction of knowing too that the surgical service is working happily and that the limitation of surgical procedures to a very few men instead of to a large number is going to produce, in a few years, a group of really well-trained surgeons. Our appreciation and indebtedness to our directing surgeon are very great. We know that above all his goal is to have at the Burbank Hospital a high degree of *surgical conscience* and that goal is being realized.

Similar constructive moves have been arranged in the various other fields of activity, — medical, obstetrical, and urological, — so that the professional resources, as a whole, offer the patients of this and surrounding communities a large measure of security and protection. A strong and outstanding consulting staff is playing a most important and generous part. These men come willingly at any time from Boston or elsewhere when needed, whether the patient is paying or not — thus establishing a cycle of care for the patient equal to any of the large hospitals. Such a program necessarily calls for high standards with adequate personnel and equipment in the several hospital departments, and steps to this end have already been and are being made.

A suggestion has been made to each active member of the hospital staff that during the coming year a certain amount of time spent at various medical centers in postgraduate work in the particular field of individual interest would be most desirable and valuable, such effort being beneficial both to staff and hospital. Several men in the surgical group are already doing such work a day a week during the more convenient season. The anesthetist and roentgenologist have taken similar steps. It is hoped the same plan may appeal to the other services.

RICHARD BULLOCK, *Directing Trustee.*
Burbank Hospital,
Fitchburg, Mass.

PURE FOOD, DRUG AND COSMETIC LAWS

To the Editor: In the *Journal* for May 12, 1938, there appeared an editorial entitled "Pure Food, Drug and Cosmetic Bill," which pointed out that, as recommended by the House Committee on Interstate and Foreign Commerce, the bill governing pure food, drugs and cosmetics was very undesirable as concerned Section 701 (f) governing enforcement, and opposition to this was urged. Subsequently the House passed the bill containing this section, but in conference this objectionable feature was so greatly modified as to render the bill highly desirable. The conference report was adopted, and in this new form the bill passed both the Senate and House and now has been signed by the President, with the result that the Food and Drug Administration of the United States Department of Agriculture will now operate under laws that greatly improve the situation as regards pure foods, drugs and cosmetics.

The remaining unsatisfactory feature in legislation concerning pure foods, drugs and cosmetics seems to lie in the control of advertising. It is possible that the Wheeler-

Lea Act, referred to editorially in the *Journal* of May 19, 1938, may work better than now seems probable. If not, the medical profession must work for the passage of a more effective bill.

It is important that physicians co-operate with the Food and Drug Administration in the enforcement of this new legislation, even if certain features, which are actually necessary for enforcement, may bring some inconvenience to individual members of the medical profession.

HENRY A. CHRISTIAN, M.D.

Peter Bent Brigham Hospital,
Boston.

ABUSED CLAIMS

To the Editor: In past years the railroad companies paid tremendous sums of money for claims for "railway spine" and "malposition of the uterus" resulting from accidents.

The present generation of attorneys have developed other much overworked conditions to justify their prosecuting claims demanding a liberal settlement or a large award in court. There are three such conditions about which there is a very great difference of opinion among the medical and legal profession; although terribly hackneyed and worn threadbare, they are constantly being used in court. The first and perhaps most abused claim is for a "concussion of the brain" with a "postconcussive syndrome"; the second, "injury to the sacroiliac joints"; the third, "aggravation of a pre-existing arthritis."

Your journal could render a great service to the medical and legal professions, as well as to the public, by submitting questionnaires to the members of the Massachusetts Medical Society as to their knowledge of these conditions and the causal relation of trauma thereto. Such a step would tend to crystallize opinion and thought, aid in adjusting automobile claims and reduce the rates of insurance.

GEORGE V. BUEHLER.

1077 Boylston Street,
Boston.

NOTICES

ANNOUNCEMENT

GEORGE E. HEELS, M.D., announces the opening of an office at 319 Longwood Avenue, Boston. Telephone, Beacon 3911.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, JULY 18

TUESDAY, JULY 19
*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

FRIDAY, JULY 22
*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

SATURDAY, JULY 23
*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Robert T. Monroe.

*Open to the medical profession.

SEPTEMBER 12-14 — American Association for the Study of Goiter. Page 545, issue of March 24.

SEPTEMBER 12-15 — American Congress of Physical Therapy. Page 946, issue of June 2.

OCTOBER 8 and NOVEMBER 15 — American Board of Ophthalmology. Page 282, issue of February 10.

OCTOBER 17-21 — Clinical Congress of the American College of Surgeons, New York City.

OCTOBER 24-26 — Academy of Physical Medicine, Scientific Session. Washington, D. C.

MARCH 27-31, 1939 — American College of Physicians. Page 36, issue of July 7.

DISTRICT MEDICAL SOCIETIES

HAMPDEN

Meeting will be held on the fourth Tuesday in July.

PLYMOUTH

Meeting will be held at 11 a. m. on July 21.

BOOKS RECEIVED FOR REVIEW

The Infant: A handbook of modern treatment. Eric Pritchard. 744 pp. Baltimore: William Wood & Company, 1938. $6.00.

The Pituitary Gland: An investigation of the most recent advances. The proceedings of the Association, New York, December 28th and 29th, 1936. Edited by Walter Timme, Angus M. Frantz and Clarence C. Hare. 764 pp. Baltimore: Williams & Wilkins Company, 1938. $10.00.

The Chemistry of the Sterids. Harry Sobotka. 634 pp. Baltimore: The Williams & Wilkins Company, 1938. $8.50.

Electrotherapy and Light Therapy. Richard Kovács. Third edition, thoroughly revised. 744 pp. Philadelphia: Lea & Febiger, 1938. $7.50.

Maternal Care Complications: The principles of management of some serious complications arising during the antepartum, intrapartum, and postpartum periods. R. D. Mussey; P. F. Williams and F. H. Falls. Edited by F. L. Adair. 95 pp. Chicago: The University of Chicago Press, 1938. $1.00

Surface and Radiological Anatomy: For students and general practitioners. Arthur B. Appleton; William J. Hamilton, and Ivan C. C. Tchaperoff. 311 pp. Baltimore: William Wood & Company, 1938. $5.50.

The International Medical Annual: A year book of treatment and practitioner's index. Edited by H. Letheby Tidy and A. Rendle Short. 615 pp. Baltimore: William Wood & Company, 1938. $6.00.

The Occupational Treatment of Mental Illness. John I. Russell. 231 pp. Baltimore: William Wood & Company, 1938. $2.50.

BOOK REVIEWS

Practical Methods in Biochemistry. Frederick C. Koch. Second edition. 302 pp. Baltimore: William Wood & Company, 1937. $2.25.

This second edition of Professor Koch's laboratory manual of biochemistry is a revision of his original manual, which was published primarily as a practical companion to Professor Mathews' textbook. It is intended entirely for the student taking up biochemistry for the first time, but contains an enormous amount of information which is easily available to the worker in the hospital laboratory. Arranged in the form of numbered experiments, the contents are divided into three parts: the chemistry of cell constituents, the chemistry of the digestive tract, the blood and urine. As to the arrangement and clearness of the directions, the book leaves nothing to be desired. It should prove a useful volume for the student or teacher in elementary biochemistry.

Leukemia and Allied Disorders. Claude E. Forkner. 333 pp. New York: The Macmillan Company, 1938. $5.00.

Until the appearance of this monograph by Dr. Forkner there has existed no comprehensive monograph on the leukemias. The author has done a remarkably thorough

bit of work in surveying the known literature on the subject. The bibliography alone is worth the price of the book. The author states that "the preparation of the manuscript has necessitated the survey of about 5000 references. The more important of these [about 1600] are cited in the text and given in full at the end of the book." Even in a hasty glance at the volume one is reassured that this statement is not an exaggerated one. The illustrations, both half-tones and colored plates, are extremely well reproduced. It is obvious that this is a monograph which will take its place as a permanent reference work and will be as useful twenty years from now as it is today.

A Textbook of Clinical Pathology. Edited by Roy R. Kracke. 567 pp. Baltimore: William Wood & Company, 1938. $6.00.

This textbook, edited by Dr. Kracke, represents a new departure in clinical pathology in that different sections and chapters have been written by various specialists. As do all textbooks of this nature, it shows a certain unevenness of contents, some chapters being extremely well done, others more mediocre in character. On occasion one notices some reduplication. The book is elaborately illustrated with photographs, line drawings and colored plates; in fact, a great many of the illustrations seem quite unnecessary, such as pictures of centrifuges, test tubes, Bunsen burners and electric lights. This, without question, makes the book more expensive than it should be. It must be confessed, however, that the photographs of high-power microscopical fields have been, on the whole, extremely well reproduced. It is questionable whether a book on clinical pathology should go as much into detail as this book does on the subject of bacteriology. Certainly the average clinical pathologist is not called upon to make diagnoses of rabies. In place of some of this material it is suggested that in future editions a chapter on the basal metabolic rate should be included, as this subject is completely ignored.

A Text-Book of Pharmaceutics. Arthur O. Bentley. Fourth edition. 1001 pp. Baltimore: William Wood & Company, 1937. $5.00.

This technical treatise on the practice of pharmacy is, in so far as may be judged by one not a pharmacist, an excellent one, though possibly the fact that it is exclusively based on the *British Pharmacopoeia* and British practice might somewhat diminish its usefulness in this country. In successive parts are considered: (1) the political history of pharmacy in Great Britain; (2) the apparatus used and the principles involved in pharmaceutical chemistry; (3) the dispensing of medicines; (4) the preparations of the *British Pharmacopoeia* and to some extent those of the *British Pharmaceutical Codex Formulary;* (5) the pharmaceutical applications of bacteriology; and (6) a survey of the principles that underlie the biologic assays of certain preparations. Of pharmacology proper — the uses of drugs and their effects in the human body — there is no discussion; as a consequence this book is only of indirect interest to the practitioner of medicine.

Histological Technique: For normal tissues, morbid changes and the identification of parasites. H. M. Carleton and E. H. Leach. Second edition. 383 pp. London, New York and Toronto: Oxford University Press, 1938. $7.25.

It seems safe to say that this book will occupy a prominent and valuable place in the working library of teachers, students, and members of the profession who desire to keep abreast of present-day histological research. It is a practical book containing in compact form the chief methods employed in the microscopic examination of human and other mammalian organs, and embodies many changes and reflects the advances in the field of technic since the first edition of 1925.

The content of the book is divided into five parts. Part I deals with the cell as a structural and physicochemical entity and with methods employed in histology such as the smear technic, vital staining, microincineration, microdissection, and so forth. Part II describes the type methods of normal histology, carrying them through the steps of dehydration, embedding, sectioning and staining. Part III treats interestingly but briefly with the accessory methods of examination by dark-ground illumination, histochemical tests and injection methods. Part IV considers the methods for special organs, tissues and cell components. Part V discusses the technic of morbid histology, including methods for the identification of micro-organisms and other parasites.

Special attention should be drawn to the following features which will prove valuable to beginners in this subject. First, there is a synopsis of recommended methods for general histology in the front inner cover of the book. Secondly, there is the useful table (page 56) of faults in dehydration, clearing and embedding, including diagnosis and remedy. Thirdly, there is the valuable table (page 78) of errors in section cutting and their remedy. Fourthly, one finds many notes and hints scattered throughout the book to save both time and effort. A final word must be said for the instructive and clear presentation of Chapters 6 and 7, written by Frederick Haynes, which deal with the general outline of the theory and practice of staining.

The reviewer feels that those who have occasion to use this book will decide that it should always be available for ready reference.

Clinical Chemistry in Practical Medicine. C. P. Stewart and D. M. Dunlop. Second edition. 372 pp. Baltimore: William Wood & Company, 1937. $4.00.

The scope of this little volume is well summarized by a quotation from the preface: "It is not an elaborate textbook of biochemistry for the laboratory worker, but it aims at something more than a short description of side-room methods, or the interpretation alone of laboratory results. It does not attempt a comprehensive account of the well-nigh innumerable tests which have been proposed at one time or another for investigating the various bodily functions; it selects those which are more important, and which, in the authors' experience, have proved useful and reliable. There are, indeed, a number of branches of the subject on which the book does not touch, but the authors' aim has been rather to treat adequately, within a small compass, the more everyday problems requiring chemical investigation, than to produce an exhaustive treatise on the capabilities of the biochemical laboratory in medicine. They have attempted further to explain the rational foundation of the tests in the hope that such an explanation will help in understanding the mechanism of many of the pathological processes concerned."

The only criticism which might be levelled at this work is that the authors do not confine themselves to the subject matter of clinical chemistry, unless the term "chemistry" may have a much broader definition than one is usually accustomed to give it. For instance, the chapter on the basal metabolic rate would hardly be termed clinical chemistry and yet a discussion of the subject is so frequently missing in many other textbooks that it seems pertinent

to include it in a work of this nature. In the appendix, too, there are sections devoted to clinical microscopy, which are not, strictly speaking, chemical examinations. In general, however, the book should prove useful, although its title might be changed from "clinical chemistry" to "clinical pathology."

Pharmaceutical Latin: For pharmaceutical, medical, dental and veterinary students and practitioners. Jacob S. Dorfman. Second edition. 146 pp. Philadelphia: Lea & Febiger, 1938. $2.00.

This little book has been prepared for those students and practitioners of medicine, dentistry, pharmacy and veterinary medicine who have had little or no Latin in their schooling. Proficiency in onomatology and prescription writing is the author's avowed object. To this end the subject has been well covered, and the man who studies the text sufficiently to be able to answer the numerous test questions should be at no embarrassing loss in the writing or reading of prescriptions. The Latin-English and English-Latin glossaries at the back are excellent for repeated reference.

On Thought in Medicine. Hermann von Helmholtz. 27 pp. Baltimore: The Johns Hopkins Press, 1938. 75c.

The editor of the *Bulletin of the Institute of the History of Medicine,* Dr. Henry E. Sigerist, is to be thanked for making available, at a nominal cost, this highly interesting and instructive lecture. Students of medical science will find in this book much of historical value; further, many of the ideas expressed by Helmholtz could be applied to the understanding of current problems in medical education.

Readers of this book will be especially interested in the date of the lecture, aside from the thesis which is being defended. The period around 1877 was one of fermentation, of the fight between learned tradition and the new spirit of natural science. In those days metaphysical nonsense was still sharply discussed; tools such as microscopes were scarce and costly; technics were few; great regard was held for method in the form of logic and metaphysics. The older philosphers and physicians believed that they could deduce before they had settled their general principles by induction. They forgot that a deduction can have no more certainty than the principle from which it is deduced; and that each new induction must be, in the first place, a new test, by experience, of its own bases. Medical education was founded mainly on the study of books; there were no physiological and physical laboratories in which the student himself might go to work.

It was into this atmosphere of false standards and ideals in science that Helmholtz entered to drive home certain fundamental points. For example, he called attention to the fundamental error in the conception that it is possible to build a complete system, which embraces all forms of disease and their cure, upon one such simple explanation as the solidar pathology or the humoral pathology. Neither is the concept of the "Archeus" of Paracelsus or the "soul of life" of Stahl adequate to explain all disease. He defended the thesis that it is a natural error to believe that thought can be liberated from its natural basis, observation and perception, to begin its Icarian flight of metaphysical speculation.

Von Helmholtz made far-reaching comments on two matters of vital importance in present-day medicine. Regarding the matter of priority of publication, he wrote: "To settle the present kind of questions of priority by the date of their first publication and without considering the ripeness of the research, has seriously favoured the mischief." He penned the following words concerning the matter of antivivisection: "But don't think that the struggle is at an end. As long as there are people of such astounding conceit as to imagine that they can effect, by a few clever strokes, that which man can otherwise only hope to achieve by toilsome labour, hypotheses will be started which, propounded as dogmas, at once promise to solve all riddles."

Professor Arno B. Luckhardt, who wrote the introduction to this book, emphasizes the interesting fact that Helmholtz made several major discoveries in the medical sciences as the outcome of his teaching activities in the field of physiology.

This thought-provoking book should be in the library of every student of medical science.

Vade Mecum of Medical Treatment. W. Gordon Sears. 368 pp. Baltimore: William Wood & Company, 1937. $4.00.

This is a convenient small book devoted to treatment listed under the names of diseases or important symptoms. It is based on English sources and some of the prescriptions contain preparations and dosages not familiar to American physicians. The book is up to date and should prove useful to practitioners of medicine, provided they are willing to accommodate themselves to the English point of view.

Play and Mental Health: Principles and practice for teachers. John E. Davis. 202 pp. New York: A. S. Barnes & Company, 1938. $2.50.

The author is well known for his previous work on recreational therapy for the mentally ill. In the present book he applies his well-known principles to children and outlines the various kinds of play which may be inaugurated by a skillful teacher. The book is well written and should appeal to physicians and teachers who have under their care children who are mentally abnormal.

Sex Satisfaction and Happy Marriage. Alfred H. Tyrer. 160 pp. New York: Emerson Books, Incorporated, 1938. $2.00.

This little book by an Episcopalian clergyman gives information in regard to sexual relations not ordinarily found in textbooks of medicine. The advice is sound, and in general, the book is well written. There is a good deal of detail which seems to be of doubtful value, considered strictly from the medical point of view.

Bile: Its toxcity and relation to disease. O. H. Horrall. 434 pp. Chicago: The University of Chicago Press, 1938. $4.00.

The contents of this book reveal a broad understanding of the modern knowledge of the composition and physiological action of bile. Essentially stimulating to the reader, it correlates and elucidates some of the clinical symptoms that appear in jaundice and offers to the physician sensible therapy in the treatment of patients with such a disease. The book is unencumbered by too descriptive biochemistry and its technical ramifications but rather presents the underlying principles involved in the formation of bile and bile physiology. Dr. Horrall has further presented a most concise and comprehensive bibliography of 2077 references, which is of considerable value.